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PRESIDENTIAL ADDRESS

Responsibility

FIRST, let me take this opportunity to express my appreciation of the office to which you have elected me. It is indeed a privilege to serve this organization in any capacity, and an honor of which I am keenly aware to have been chosen your President.

I would add my grateful thanks to the various officers of this Association who so ably conduct the affairs of this society and to the members of the local committee who have carried the burden of arrangements for this meeting, and to all of you for the continued cooperation and interest that make the meetings of this group so stimulating.

The last meeting of this Association at which the Washington members were host was held in Seattle and Harrison Hot Springs in 1953. That was the first meeting of this Association at which newly elected members from British Columbia were in attendance. It is gratifying, indeed, to see our membership across the border flourish, extending a closer bond of friendship and understanding between surgeons of the two countries.

The extension of our membership into British Columbia was simultaneous with our increased membership in general, and was the outcome of a reorganization of this Society, completed in 1950. The rapid industrial expansion on the Pacific Coast during and immediately after World War II, coupled with a marked increase in the population, attracted many young, well trained surgeons to this area. The extended activities of the older medical schools on the Coast, and the development of three new schools, were an added source of attraction. Keenly aware of these developments and the necessity of reorganization of the Pacific Coast Surgical Association, Howard Naffziger offered in his Presidential Address in 1949, specific recommendations for change.

I will not dwell on the thoughtful efforts involved in the revision of the Constitution and By-laws which activated Doctor Naffziger's recommendations except to comment on the wholehearted interest and cooperation of everyone in accomplishing these necessary and beneficial alterations. The especially helpful changes included an enlargement of the membership, extension of the scientific program from three sessions to five, and the election of a recorder to arrange and supervise the scientific program.

This same stimulating interest and cooperation on the part of the members is also responsible for the excellent scientific programs we have enjoyed and indicates a high sense of responsibility to the Association that is recognized by all its members.

It may be presumptuous of me to speak to this group on the subject of responsibility of membership. However, a discussion of some of the salient features having to do with the strength and significance of a surgical society, this one in particular, and some of the pitfalls to success may bear some fruit.

The strength and appeal of this Association lies in three major areas, each of which contributes not only to the purpose of our existence but also to the prestige of the organization and to the high place it holds in our esteem.

The first of these areas of significance is the scientific program. The extended and unselfish efforts of our first recorder, Tom Berne, now

ably succeeded by Lyman Brewer, have been most fruitful; and well rounded programs and free discussion have been drawn almost entirely from our own membership. This high degree of membership participation, the essence of a stimulating scientific program, perhaps the greatest single factor in maintaining keen interest in a society, and one of our greatest attributes, is not enjoyed by all surgical groups and is not desired by some. For example, at a recent meeting of a national surgical association, the official program shows that of a total of thirty-six papers, only twenty represented some effort on the part of a member of the society. Only eight papers were presented by a member. Twelve papers were given by a non-member with a member's name on the paper. Sixteen of the thirty-six papers were presented by a non-member, sponsored by a member whose name was not on the paper. Only twenty papers then, little more than half the program, represented some effort by a member of the organization.

The selection of material for an annual meeting in the manner just described, may make for an excellent program and may meet the goal of some particular organization, but it does limit free discussion and exchange of opinion. In a surgical society such as ours I can only believe that such a practice, if instituted, would soon lead to meager support of the recorder by the membership and an early loss of interest in the society and its function.

I see no objection to the presentation of a paper by a non-member of a society when such a paper represents a combined effort, and particularly when co-authors, who are members of the society, are present to contribute to the discussion. Such a practice need not detract from membership contribution to and participation in a scientific program but rather may add to it.

Since evidence of the interest and ability to contribute to scientific discussion is required of all candidates for membership, a lagging interest in the annual program, and in other society matters as well, suggests either too many commitments on the part of the individual, unawareness of, or disregard of, the responsibility imposed by membership.

The outstanding individual, the productive investigator, the teacher of surgery, are eagerly sought by all societies. Their cooperation is essential to the structure, the function and the scientific program of a group such as this. The resources available to such individuals are more than adequate for contributions in support of multiple responsibilities.

Others, whose productivity may appear limited, should have an abundant source of clinical material for scientific discussion if they would utilize it. To others, whose resources are limited, the urge for recognition through society membership should be controlled by an awareness of the responsibilities imposed by such membership, and this awareness must apply to the applicant, to his sponsors and to the Council.

John Milton in his Areopagitica in 1644 said, "Where there is much desire to learn, there, of necessity, will be much arguing, much writing, many opinions; for opinion in good men is but knowledge in the making." Where can the writings and arguments be better presented and the opinions better expressed than before an interested and selected group who present their own arguments and develop their own opinions?

Apart from the scientific program, a significant feature of our annual meeting has been social activity, stimulated and delightfully embellished by the presence of our wives at these annual gatherings. The planned and the spontaneous moments of relaxation have served not only to cement friendships and broaden our contacts, but by these means also add some stimulus to the free discussion of scientific matters. This happy combination of scientific discussion and social entertainment is an old and well established tradition in this society and will, I hope, never be discarded.

A second area of strength of this Association is the broad base of membership. The faculties of all the medical schools along the Coast are well represented, as well as the part time teacher and the private practitioner of surgery. The backbone of our membership, quite properly, is the general surgeon, well and wisely supported by representatives of the surgical specialties. It is only with continued and thoughtful concern on the part of the members and the Council that this productive and proper relationship can be maintained. This happy combination, equitably representing the teacher, the investigator and the practitioner of both general and specialized areas of surgery not only makes for better balanced programs and broad discussions, but adds to our strength, and above all, avoids the risk of becoming a counterpart of some other organization.

A final factor in our strength is the equitable distribution of society control in the four geographical areas represented. This particular method of management of society affairs is unique, and has served us well. It prevents society control from slipping into the hands of a small self-perpetuating group; it gives the constituent groups a voice in society affairs; it gives the local group a strong voice in the selection of new members from its own territory; and adds, I believe, a great stimulus to individual interest in the organization. For this type of society control to be effective, a double responsibility is placed upon the Counselor in each area. Thoughtfulness, interest and leadership on his part at the local level can be a bulwark of strength to the Association.

These are the factors then that have contributed to the strength of this society and must be reckoned with in the future if the present identity and purpose of the organization is to be retained. What of the future?

Population growth, a major factor bringing about our reorganization in 1950, continues unabated. Between 1950 and 1955 while population in the rest of the country increased 7 per cent, in the West it increased 18½ per cent, and most of this increase occurred along the Pacific Coast.

In 1975 it is estimated that the Western States will have approximately 70 per cent more inhabitants than they had in 1955. It is further projected that the majority of this growth will occur about urban areas, with the greatest increase along the Pacific Coast, notably in California.

This vast increase in population, as it develops, will require more medical schools and greatly expanded training facilities in order to meet the demands of the expanding population. There will come also, demands for additional surgical societies or great expansion of those that already exist. Let us hope the membership of this organization may never grow to a point where its present attributes are jeopardized. Some other organization now in existence, or one yet to be formed, may better meet the needs of the increased numbers of surgeons located up and down the Coast.

In this day of rapid progress, extraordinarily keen competition, and the magnificent subsidy extended in many walks of life, the fruits of labor are too often taken for granted. Too much reward is anticipated too quickly, by too many. The influence of this "something for nothing" philosophy is seen in many young people today, and in many men early in their surgical experience. A sense of obligation and a mature appreciation of relative values, both essential to the support of an organization, may not be too quickly acquired under these current influences.

I have not considered it presumptuous to speak to this present group on the responsibilities of membership and the qualities of real value in our society because it is we who are the trustees of this association and it is our responsibility to preserve the elements of strength inherent in our present organization. We must perpetuate a thoughtful and responsible membership dedicated to argument, expression of opinion and free discussion of surgical matters.

These comments may be of some value to those yet to enjoy Fellowship in this society, those who will be the trustees of the organization in years to come.

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Open Reduction of Fractures and Dislocations of the Ankle

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MOST closed fractures and dislocations of the ankle region can be treated successfully by closed technics. If anatomical reduction cannot be achieved and maintained until healing is sound, the onset of disabling symptoms of post-traumatic arthritis may be accelerated. When closed technics are unsuccessful, the onset of symptoms may be delayed by open reduction and fixation by a combination of internal and external means.

For optimal results, most open fractures and dislocations of the ankle joint require initial excision wound surgery. Primary closure of the joint cavity may assist in the prevention of septic arthritis. This may be aided by accurate fixation of the fracture and careful repair of damaged ligaments.

The purpose of this discussion is to consider, from a practical point of view, the operative treatment of common, acute fractures and dislocations of the ankle joint in the adult. Fractures of the astragalus are not included.

CLASSIFICATION

Fractures and dislocations of the ankle joint, apparently caused by indirect violence, frequently produce "typical" lesions. In an extensive historical review of fractures of the ankle, Lauge [*10*] commented in 1948, "The classification of malleolar fractures in the literature is almost chaotic." Subsequently, he offered a classification that divided these injuries into five major categories with seventeen subtypes [*11,12*]. Most classifications are based upon a mechanistic etiology. The mechanogenesis has been determined by comparing fractures and dislocations presumably caused by indirect violence in patients to similar lesions that have been produced experimentally in cadavers by stresses of known direction. Since the forces and moments used to produce these experimental lesions were generally simple and their order of magnitude as well as the rate of absorption of applied energy have not been recorded, the assumptions that such conditions pertain to clinical injuries rested in a great measure on speculation. Furthermore, the experimental lesions have been produced entirely by extrinsic stresses, disregarding the intrinsic ones due to muscle activity.

The type and location of mechanical failure, fracture or ligamentous rupture depends in part upon the relative strengths of the tissues of the person. From the point of view of open operative treatment, the complex dynamic stresses of extrinsic and intrinsic origin may cause such a variety of combinations of osseoligamentous injuries to the ankle joint that they would defy a definitive but practical classification. In those injuries commonly attributed to indirect violence, the direction and magnitude of maximal spatial displacement of the astragalus in reference to the tibia may be correlated with the degree and type of osseous and ligamentous injuries. A precise understanding of the functional anatomy of the ankle region coupled with certain diagnostic criteria can determine with a fair degree of certainty the single or combination of lesions amendable to

operative treatment. Classification then becomes more an academic exercise than a matter of practical necessity for successful operative management.

DIAGNOSIS

An accurate diagnosis is essential in those injuries likely to require open operation, in order to plan surgical approaches and methods of fixation. Careful physical examination combined with roentgenographic study under conditions of maximal displacement give reasonably accurate information in regard to the extent of gross lesions. The type and extent of osseoligamentous injury is suggested frequently by the causative trauma. The extent of manipulation and type of emergency splinting prior to the initial roentgenographic examination may modify the magnitude of the original displacement. The degree and direction of displacement of the foot in relation to the leg may indicate the severity and extent of the injuries.

The time lag between injury and definitive treatment is not only of importance for open injuries but also for the timing of operative treatment of closed injuries. The presence of complicating or associated injuries may determine the timing of operative treatment. For example, an open fracture-dislocation of the ankle joint should receive treatment before an associated, undisplaced fracture of the forearm but should not receive priority over a sucking wound of the chest. Complicating local vascular or nerve injuries may be factors in determining the selection of open treatment. The condition of the skin and underlying soft tissues have important bearing on the selection of treatment. The presence of extensive soft tissue swelling, blebs, and ringworm infections may influence the selection of initial treatment.

Adequate roentgenographic examination and interpretation are of importance to establish a precise diagnosis and to plan proper operative treatment. A comprehensive understanding of the functional anatomy of the talocrural and tibiofibular articulations is necessary for the accurate interpretation of roentgenograms. The roentgenograms must be of the best technical quality. Inadequate roentgenograms are a certain step toward incomplete diagnosis and unsuccessful treatment. X-ray films should be exposed in a sufficient variety of projections to demonstrate the extent and configuration of all major fragments of the fracture. In addition to the customary anteroposterior, lateral and 30-degree internal oblique projections, other oblique projections must be made in case of question. Roentgenograms should demonstrate clearly the relations of articular surfaces. Wide separation of articular surfaces is not necessary for interposition of important structures of the soft tissue. (Figs. 1A through C.) In case of uncertainty, comparison of the uninjured opposite joint may give additional information.

FIG. 1. A, March 18, 1957. A thirty-three year old man. Anteroposterior and lateral roentgenograms demonstrate a fracture of the lateral malleolus. The relation of the medial malleolus to the astragalus was not clearly demonstrated. B, March 18, 1957. A slightly different anteroposterior projection reveals lateral displacement of the astragalus. C, March 10, 1958. One year after injury. The deltoid ligament and posterior tibial tendon were found interposed between the medial malleolus and the astragalus at the time of operation. Anatomical restoration has been accomplished by fixation of the malleolar fracture and repair of the deltoid ligament.

The initial roentgenograms may indicate the minimal and not the maximal degree of displacement. Definite indications for stress roentgenography cannot be given [8,9]. The initial examination may demonstrate satisfactorily extensive displacement and the configuration of the fragments. (Figs. 2A and B.) Further examination of such lesions after strain would demonstrate little more. From the

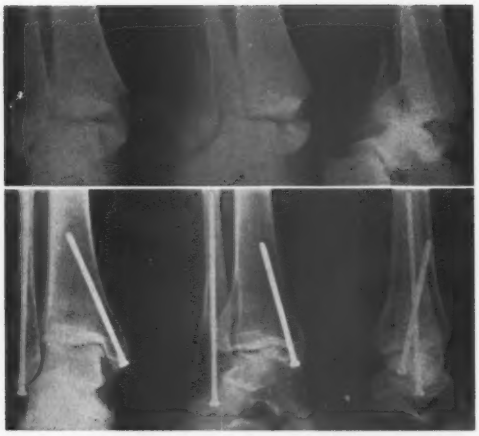


FIG. 2. A, June 12, 1950. A forty year old woman. Closed fractures of both malleoli and the posterior tubercle of the tibia, and dislocation of the ankle joint. B, March 10, 1955. Five years later, the patient had slight restriction of dorsiflexion and mild symptoms compatible with post-traumatic arthritis.

practical point of view, little additional information can be derived from stress roentgenography when there is minimal swelling of soft tissues, minor subjective complaints and no displacement. Stress roentgenography may give significant information when doubt exists (Figs. 3A through C.) Since these examinations frequently require anesthesia, they should be planned, if possible, as an immediate preliminary to open or closed treatment.

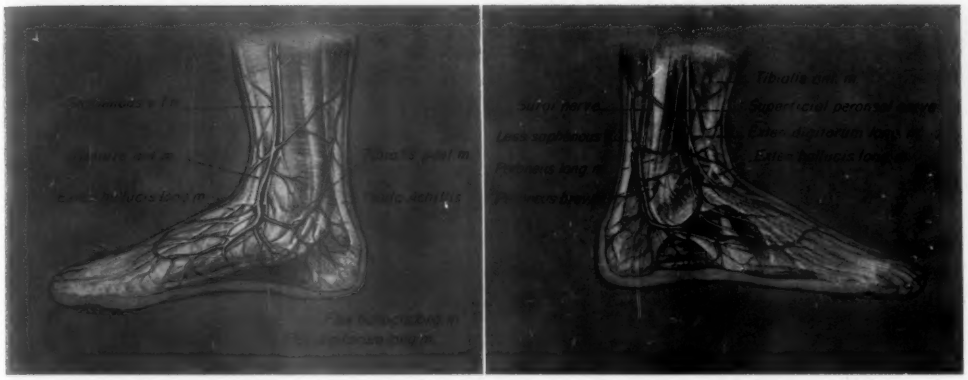
INDICATIONS FOR OPEN TREATMENT

The most common indication for open reduction and internal fixation of closed fractures of the ankle joint is the inability to achieve anatomical reduction by closed manipulation and to maintain it until healing is sound [*3,5,13*]. The incidence of post-traumatic arthritis has been reported to be greater among those patients with inaccurate reductions [*17*]. De Marneffe [*7*] has found the period of rehabilitation shorter among those patients who underwent open reduction than among those who did not.

Open treatment should be attempted only by those who are acquainted with the general principles of internal fixation of fractures and the management of the complications that are likely to occur.

Extensive swelling due to edema and hemorrhage are associated with severe injuries about the ankle joint. Where swelling is severe, bleb formation is likely to occur. Therefore, when open reduction is necessary, it should be performed as soon after injury as possible. Open reduction should be deferred until blebs, abrasions of more than a few hours' duration, and cutaneous infections have healed. It may take a month to prepare the skin adequately, but such delay can be justified to prevent operative wound infection. Moderate soft tissue swelling may be temporarily dispersed at the time of operation by applying a snug rubber

FIG. 3. A, December 30, 1950. A thirty year old man. Routine roentgenographic studies demonstrated only minimal displacement of a fracture of the lateral malleolus. B, December 30, 1950. Stress roentgenography showed lateral and transverse torsional displacement of the astragalus. C, July 15, 1955. Four and a half years following fixation of the malleolar fracture and repair of the laceration of the mid-portion of the deltoid ligament, the patient only complained of an inclement weather ache. A similar gratifying result might have followed closed treatment.



4A 4B

FIG. 4. A, the relation of the great saphenous vein and saphenous nerve to the medial aspect of the ankle. B, relation of the small saphenous vein, and the sural and superficial peroneal nerves to the lateral aspect of the ankle.

bandage to the foot and leg prior to performing the skin incision. It is prudent to combat severe swelling by preliminary closed manipulation, the application of a compression dressing, and elevation for a few days.

SURGICAL APPROACHES

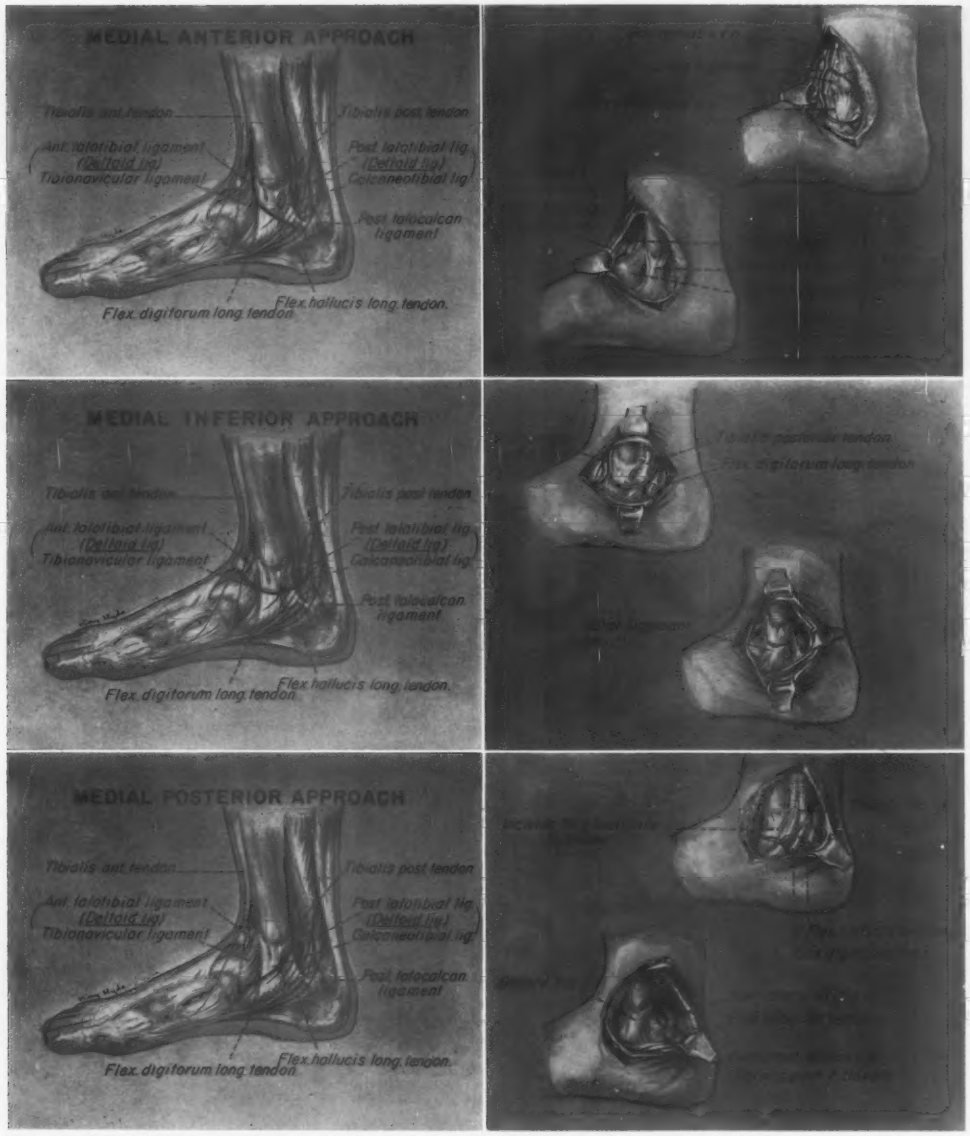
Bonnin [*1*] has discussed in detail the surgical anatomy of the ankle region. Others [*4,8,14,15*] have emphasized the importance of the function of ligaments about the ankle and their relation to pathological movements following injury.

Of the many surgical approaches to the ankle joint, five basic paramalleolar approaches have been found to be of special value for the open treatment of the major proportion of closed fractures and dislocations. The advantageous route, anterior or posterior to the malleolus, is determined by the location and extent of osseo-ligamentous injury. Injury to certain superficial veins and cutaneous nerves can be avoided by proper planning and execution of the surgical approaches. (Figs. 4A and B.)

The Medial Anterior Approach. The medial anterior approach serves for exposure of fractures of the medial malleolus. (Figs. 5A and B.) The longitudinal part of the skin incision is started 3 fingerbreadths above the tip and over the anterior margin of the malleolus. The incision is extended distally to the joint level where it is curved gently backward, passing 1 fingerbreadth below the tip and stopping at a point directly below the posterior margin of the malleolus. The great saphenous vein and terminal branches of the saphenous nerve lie anteriorly in the subcutaneous fat. Only tributaries of the vein are encountered as the fatty superficial fascia is divided in the direction of the skin incision. (Figs. 4A and B.) Limited undermining gives exposure of the malleolus and superficial fibers of the deltoid ligament. (Fig. 5B.) The sheath of the posterior tibial tendon covered by the laciniate ligament lies deep in the distal extremity of the exposure.

The Medial Inferior Approach. The medial inferior approach gives access to lesions of various components of the deltoid ligament. (Figs. 6A and B.) The crescent incision of the skin and fat is started 1 fingerbreadth above the tip and a scant fingerbreadth in front of the malleolus. It is extended posteriorly in a convex inferior arc, the center of which reaches 1 fingerbreadth below the malleolus, to terminate 1 fingerbreadth above the tip and a scant fingerbreadth behind the malleolus. The great saphenous vein is found in the fat in the anterior extremity of the exposure. (Fig. 6B.) The sheath of the posterior tibial tendon lies deep, beneath the laciniate ligament, posteriorly. Only limited dissection over the deltoid ligament is necessary to give adequate exposure to the superficial fibers of all its components. (Fig. 6B.) It is necessary to divide the laciniate ligament and the sheath of the posterior tibial tendon to expose the posterior talotibial ligament, the deep component of the deltoid ligament. (Fig. 7B.)

The Medial Posterior Approach. The medial posterior approach is useful for exposure of fractures of the posteromedial aspect of the



5A 5B

6A 6B

7A 7B

FIG. 5. A, the medial anterior approach. The relation of the skin incision to the underlying tendons and ligaments. B, the relation of the skin incision to the great saphenous vein and saphenous nerve. Retraction of the wound margins brings into the view the superficial fibers of the deltoid ligament.

FIG. 6. A, the medial inferior approach. The relation of the skin incision to the deltoid ligament and the medial malleolus. B, the wound margins have been retracted demonstrating the great saphenous vein and saphenous nerve anteriorly, and the long flexor tendons posteriorly. Deeper dissection after division of the laciniate ligament and the sheath of the posterior tibial tendon demonstrates a tear of the calcaneotibial component of the deltoid ligament in the mid-portion.

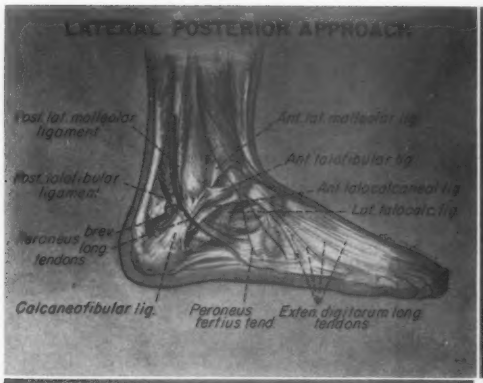
FIG. 7. A, the medial posterior approach. The relation of the skin incision to the medial aspect of the distal extremity of the tibia, the long flexor tendons and the deltoid ligament. B, the direction of the incision of the laciniate ligament and the sheath of the posterior tibial tendon. Retraction of the posterior tibial tendon demonstrates the posterior talotibial ligament and the deep fibers of the deltoid ligament.

8A 8B

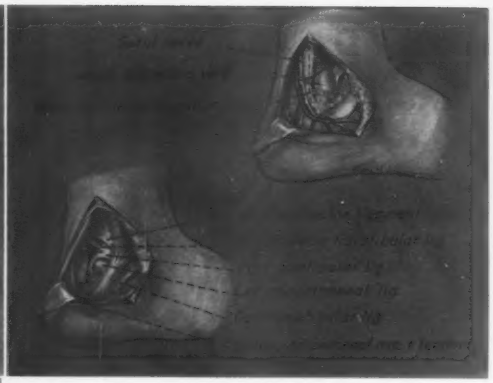
FIG. 8. A, the lateral anterior approach. The relation of the skin incision to the lateral malleolus and to the major ligaments of the lateral aspect of the ankle region. B, the direction of the incision of the crural ligaments and the relation to the branches of the superficial peroneal nerve and the perforating peroneal veins. Retraction of the long extensor tendons demonstrates the anterior lateral malleolar and the anterior talofibular ligaments.

distal extremity of the tibia. (Figs. 7A and B.) Such fractures frequently extend into the medial malleolus and may be associated with lesions of the deltoid ligament. (Figs. 15A and B.) The prone lateral decubitus positions may facilitate the exposure. The longitudinal component of the incision lies over the posterior margin of the distal extremity of the tibia. The proximal extent is determined by the fracture. The incision of the skin and fat is carried distally to the level of the joint where it is curved gently anteriorly to pass 1 fingerbreadth below the tip, ending at a point directly below the anterior margin of the malleolus. The posteromedial aspect of the distal extremity of the tibia may be exposed subperiosteally without entering the deep posterior muscle compartment by incision of the tibial periosteum directly beneath the longitudinal component of the skin incision. In order to preserve the periosteal attachment of fracture fragments, extraperiosteal exposure is accomplished by entering the deep posterior muscle compartment. Proximally, the intramuscular septum is divided close to its attachment to the tibia. Distally, it is necessary to incise the laciniate ligament and the sheath of the posterior tibial tendon. (Fig. 7B.) The dissection should be developed close to the periosteum. Plantar flexion of the foot facilitates retraction of the posterior tibial tendon and exposure of the posterior talotibial ligament as well as the adjacent joint capsule.

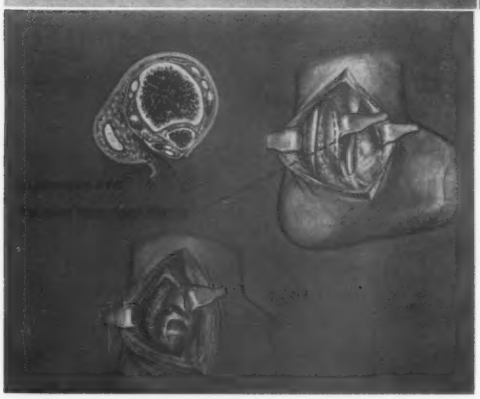
Lateral Anterior Approach. In this experience, fracture of the lateral malleolus has been the most frequent single lesion among those requiring open operation. The lateral anterior approach has served well to expose not only the malleolus but also the anterior lateral malleolar, the anterior talofibular and the calcaneofibular ligaments. It gives adequate access both to the tibiofibular joint when fracture of the malleolus is associated and to the anterolateral aspect of the ankle joint. The longitudinal component of the incision of the skin and subcutaneous tissue lies over and is parallel to the anterolateral margin of the shaft and malleolus. (Figs. 8A and B.) The proximal origin of the incision depends upon the extent of the fracture of the lower fibula or tibia. The incision is carried distally to the level of the ankle joint where it curves gently backward, to pass a scant fingerbreadth below the tip and ending at a point directly below the posterior margin of the malleolus. The lateral branch of the superficial peroneal nerve lies in the subcutaneous fat in the anterior part of the exposure. (Fig. 4B.) A smaller and inconstant branch separates from the main trunk somewhat distal to the point where it perforates the fascia in the middle third of the leg. This small branch lies in the fat and courses distally, parallel to the lower shaft of the fibula, to ramify in the area of the malleolus. Injury to this branch may account for the occasionally annoying and tender scar following a longitudinal incision over the center of the lower fibula. Dissection of the skin posteriorly gives access to the



9A



9B



9C

FIG. 9. A, lateral posterior approach. The relation of the skin incision to the lateral malleolus, peroneal tendons and calcaneofibular ligament. B, the direction of the incision of the peroneal retinacula and the sheaths of the peroneal tendons in relation to the sural nerve and small saphenous vein. C, the direction of the approach between the sural nerve and small saphenous vein, and the peroneal tendons. The direction of the incision of the intermuscular septum medial to the peroneus brevis.

malleolus. (Fig. 8B.) The fibular attachment of the transverse crural ligament and the crural fascia are divided close to the fibula in order to free the tendons of the peroneus tertius and the extensor digitorium longus. By maintaining the dissection close to the periosteum anteriorly, the anterior lateral malleolar ligament is exposed. The small perforating peroneal artery may require ligation. The sural nerve and small saphenous vein are encountered in the fat in the lower extremity of the incision. In order to gain access to the calcaneal attachment of the calcaneofibular ligament, it is necessary to incise the inferior retinaculum and retract the peroneal tendons. (Fig. 9B.)

Lateral Posterior Approach. The lateral posterior approach permits exposure of the posterolateral aspect of the distal extremity of the tibia, adjacent ankle joint capsule and the posterior aspect of the tibiofibular joint. The operation can be made easier by placing the patient in either the prone or lateral decubitus position. The longitudinal component of the skin incision lies over the posterior margin of the lower fibula and its proximal origin is determined by the extent of the fracture. (Figs. 9A and B.) It is carried distally to the level of the ankle joint where it curves anteriorly to pass a scant fingerbreadth below the tip, and to end at a point directly below the anterior margin of the malleolus. Careful dissection of the fatty superficial fascia will avoid injury to the small saphenous vein and sural nerve which lie posteriorly in that structure. (Fig. 9B.) Transverse tributaries of the vein are encountered at the level of the malleolus. (Fig. 4B.) Above the level of the ankle joint, the dissection is developed medially close to the intermuscular septum that covers the peroneus brevis muscle and tendon. (Fig. 9C.) On the medial aspect, the intermuscular septum is divided longitudinally, exposing the fatty interval between the peroneus brevis and the flexor hallucis longus. The fat is separated from the peroneus brevis, exposing the posterior aspect of the tibia. Distally, the thickened

portion of the crural fascia, the superior peroneal retinaculum, is divided. (Fig. 9B.) By incision of the sheath, the peroneal tendons can be retracted, exposing the posterior lateral malleolar and talofibular ligaments.

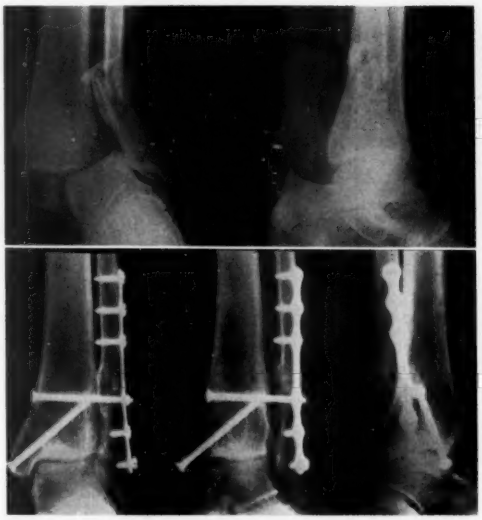
TECHNIC

General. Many technical variations and a wide selection of devices are available for the internal fixation of fractures about the ankle. The selection of design of devices for internal fixation must rest in a measure on the preferences of the surgeon. In this experience, simple, standard devices have proved to be satisfactory. A thorough understanding of the general principles of internal fixation of fractures and the meticulous attention to details of technic are of greater importance in achieving successful treatment than elaborate apparatus.

Most technics have in common the intent to stabilize the fragments with minimal injury to the articular surfaces and to permit physiological joint motion as soon as displacement is no longer feared. The precise configuration of the fragments and the degree of comminution have important bearing from this point of view.

Two general concepts of internal fixation are applicable for most fractures about the ankle joint. The one is based on the premise of the use of sufficient fixation apparatus to obviate external immobilization and to permit active motion as soon as soft tissue healing is sound [*16*]. (Figs. 10A and B.) Because of the relative thinness of the skin and the sparsity of subcutaneous fat covering the region of some ankle joints, symptomatic adventitious bursae are likely to develop over large fixation devices such as bone plates. Conversely, a generous amount of subcutaneous fat gives protection to the fixation apparatus. Current technics of internal fixation do not provide sufficient rigidity to permit unsupported weight bearing before bone healing is sound. Obviously, failure can be expected in the untrustworthy patient who disregards this admonition.

The other concept is the use of a minimum of fixation devices internally to assure stability and to place major dependency on external fixation. Technical failures commonly result from the frugal use of internal fixation apparatus. A practical compromise consists in the use of sufficient apparatus internally to permit immobilization of the foot in the neutral position and to insure stability during the critical



10A

10B

FIG. 10. A, June 9, 1951. A sixty-seven year old woman. Open fractures of the malleoli and dislocations of the ankle and tibiofibular joints. A transverse wound 8.0 cm. in length was present at the level of the fracture site medially. Following wound excision, the fractures were fixed internally. The subcutaneous tissue and skin were closed secondarily. B, August 22, 1956. Five years after injury there has been some calcification of the tibiofibular ligaments. The bolt across the tibiofibular joint has loosened.

periods of application of plaster and when loosening in the plaster takes place from the absorption of soft tissue swelling.

No firm rule can be followed in regard to the sequence of repair of multiple lesions. Generally, preliminary fixation of the fracture gives mechanical stability and simplifies suture of the ligament. Prior to closure of the wound, the competency of internal fixation and ligamentous repair should be assessed with the foot in the same position that immobilization in plaster is anticipated. Extreme positions of immobilization of the foot can be avoided if sufficient apparatus is used to assure stability and ligamentous repair has been meticulous.

Fractures of the Medial Malleolus. Isolated fractures of the medial malleolus may be exposed adequately by the medial anterior approach. (Figs. 5A and B.) Wherever associated with fracture of the posteromedial aspect of the lower extremity of the tibia and tear of the deltoid ligament, the medial posterior approach is preferred. (Figs. 7A and B.) The fracture site is exposed extraperiosteally. A

11A

11B

FIG. 11. A, October 18, 1952. A sixty year old woman. Closed fractures of both malleoli and lateral dislocation of the astragalus. B, November 6, 1957. Five years after anatomical restoration. Two screws were necessary to stabilize the large fragment of the medial malleolus. Since the anterior lateral malleolar ligament was intact, fixation of the fracture of the lateral malleolus by a single coaxial screw and a wire cerclage restored the integrity of the tibiofibular joint.

12A

12B

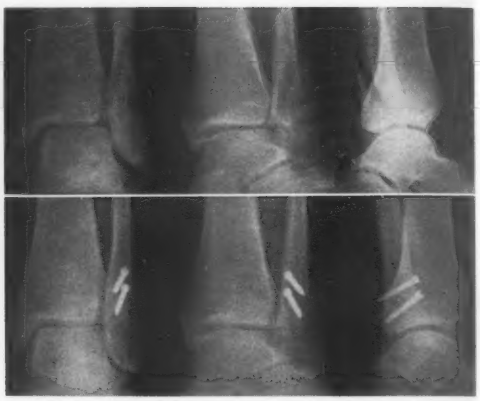


FIG. 12. A, December 22, 1955. A twenty-eight year old woman. Closed fracture of the lateral malleolus with minimal lateral displacement of the astragalus. Stress examination suggested a tear of the deltoid ligament. B, June 25, 1956. Six months after anatomical restoration. The deltoid ligament lesion was repaired. The anterior lateral malleolar ligament was intact but the posterior lateral malleolar ligament had been torn. Fixation of the non-comminuted fibular fracture by means of two small, transfixion screws restored the integrity of the tibiofibular joint.

longitudinal incision of the anterior joint capsule along the lateral margin of the anterior talotibial ligament generally will permit retraction of the distal fragment for inspection of the joint cavity. This incision of the anterior joint capsule not only permits inspection of the articular surfaces for determination of the adequacy of reduction but also demonstrates whether or not the fixation device has traversed the joint cavity. Small fragments may be stabilized by a single screw. (Figs. 2A and B.) Larger fragments may require two or even more screws to achieve reasonable rigidity. (Figs. 11A and B.) The screws should be of sufficient length to insure extensive contact with the cancellous bone of the distal tibia. A small incision is made in the tibial attachment of the calcaneotibial ligament. The length of the hole should be a few millimeters longer than the screw. A screw longer than the hole may impinge during seating, causing displacement of the fragment and loss of reduction. Counter sinking of the screw head may prevent formation of symptomatic adventitious bursae from irritation. The fracture should be held firmly reduced while the screw is being inserted.

Fractures of the Lateral Malleolus. In this experience, the most frequent single lesion to require operative treatment has been fracture of the lateral malleolus. These fractures may be exposed adequately by either the anterior or posterior lateral approach. The selection of the approach depends upon associated local fractures or ligamentous injuries. When fracture of the anterolateral aspect of the distal tibia, or when tears of either the anterior lateral malleolar or the anterior talofibular ligaments are associated, the lateral anterior approach is preferred. (Figs. 8A and B.) When fracture of the posterolateral aspect of the distal tibia, or when tears of the posterior lateral malleolar, the posterior talofibular or calcaneofibular ligaments are also present, the lateral posterior approach is more useful. (Figs. 9A through C.)

The fracture site is exposed extraperiosteally. The manner of fixation of the fragments depends in a measure on the location and configuration of the fracture, the severity of comminution, and the presence of associated injuries. If there is no complicating local injury, an oblique fracture may be stabilized by one or two small transfixion screws. (Figs. 12A and B.) If bone atrophy is present and the cortex is thin, a single, long coaxial screw may give adequate stability. (Figs. 2A and B.) Under other circumstances, further stability may be attained by the addition of one or two wire cerclages. (Figs. 11A and B.) A coaxial screw may be combined with a transfixion screw to

FIG. 13. A, December 25, 1957. A sixty-five year old man. Closed fracture of the lateral malleolus with tear of the posterior lateral malleolar ligament and lateral displacement of the astragalus. A bit of bone between the medial malleolus and astragalus suggested an avulsion of the deltoid ligament from the tibia. B, April 3, 1958. Two and a half months after fixation of the lateral malleolus with two coaxial screws and repair of the deltoid ligament lesion. Since the anterior lateral ligament was intact, the integrity of the tibiofibular joint was restored by fixation of the fibular fracture.

FIG. 14. A, March 15, 1950. A forty-five year old man. A closed comminuted fracture of the distal extremity of the tibia and fracture of the lateral malleolus. The extensive comminution defied adequate internal fixation. B, April 8, 1955. Five years after injury. Initial treatment was by traction and external immobilization, followed by arthrodesis three months after injury.

give biplane rigidity. (Figs. 3A through C.) Where transfixion screws are used, they should not extend beyond the posterior cortex of the fibula because of the proximity of the peroneal tendons. In the comminuted fracture where a cerclage or transfixion screw cannot be used to insure stability, a second, shorter coaxial screw may be added. (Figs. 13A and B.) The coaxial screw is inserted from the tip of the malleolus. A small incision is made in the attachment of the calcaneofibular ligament. The fracture is reduced and held firmly with a clamp while the hole is drilled and the screws inserted. The hole must be started exactly coaxial to the medullary cavity or the drill may perforate the cortex medially. The head of the screw should be counter sunk because of proximity of the peroneal tendons and because of its superficial position. If question exists whether or not the hole has perforated the cortex, it may be answered by inserting a fine Kirschner wire with a small hook on the end.

Fractures of the Distal Tibia. Fractures of the distal extremity of the tibia, except those involving the medial malleolus alone, are generally associated with other lesions. Fractures with extensive comminution into the ankle joint with multiple small fragments, the so-called "compression type," are not amendable to internal fixation. (Figs. 14A and B.)

Fractures of the posterior lip may involve either the entire posterior half of the distal articular surface of the tibia or segments. The approach for exposure of the fragments depends in part on the associated lesions as well as the location of the major fragment. Careful study of roentgenograms made in multiple projections is necessary to determine the most advantageous approach. When the fracture extends into

15A

15B

FIG. 15. A, April 29, 1956. A thirty-three year old man. A closed, comminuted fracture of the lateral malleolus with tear of the posterior lateral malleolar ligament, fracture of the posteromedial aspect of the distal extremity of the tibia with extension into the medial malleolus, tears of the anterior talotibial, tibionavicular and calcaneotibial ligaments. The astragalus is displaced posteromedially. B, October 17, 1956. Six months after anatomical restoration. Since the anterior lateral malleolar ligament was intact, adequate fixation of the fracture of the lateral malleolus restored the integrity of the tibiofibular joint. Insertion of screws for fixation of the tibial fractures could be accomplished more readily from the anteromedial aspect.

16A

16B

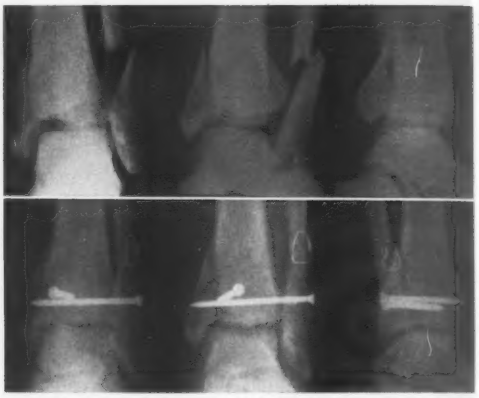


FIG. 16. A, December 9, 1955. A twenty-four year old man. One month after closed fractures of the medial malleolus and posterior lip of the tibia, and the lower shaft of the fibula. The ankle and tibiofibular joints have been dislocated. B, March 12, 1956. Four months after open reduction. The fibular fragments have been approximated by a single wire loop. The posterior lip fragment has been stabilized by a screw. Another screw maintains reduction of both the tibiofibular joint and the medial malleolus. Complete rupture of all ligaments of the tibiofibular joint was found.

the medial malleolus, the medial posterior approach is preferred. (Figs. 15A and B.) Fracture of the medial malleolus associated with fracture of the posterior lip may be exposed in the same manner. (Figs. 16A and B.) Large fragments of the lateral aspect of the posterior lip commonly include the posterior tibial tubercle and extend into the tibiofibular joint. The lateral posterior approach is advantageous. (Fig. 9C.) Both posterior approaches, the lateral and the medial, may be necessary for adequate exposure when comminution exists. (Figs. 17A and B.)

Fracture of the anterior aspect of the distal articular surface of the tibia without fracture of the posterior lip is relatively infrequent. These fractures may be exposed by either the medial anterior or the lateral anterior approach, or by a combination of both.

It is preferred to expose the fragments extraperiosteally in order to preserve capsular and periosteal attachments. Minor fragments of the posterior lip, those that are estimated to involve less than 20 per cent of the joint surface, may be disregarded if they do not prevent repair of other lesions.

Lesions of Ligaments. Lesions of ligaments that require operative repair are gross and generally involve all or a major proportion of the structures. Ligaments may be ruptured at any point between their bone attachments. Avulsion of bits of bone commonly accompany tears of ligaments from their osseous origins. (Figs. 13A and B, 17A and B.) The configuration of tears varies but characteristically the ends are frayed, making repair difficult. Complete rupture of all major ligaments of the talocrural joint with dislocation of the astragalus but without fracture is observed rarely. Generally, major ligamentous injuries about the ankle joint are associated with fractures. It is preferred to repair these lesions with multiple sutures of fine, non-metallic material.

Major lesions of the various components of the deltoid ligament may be exposed by the

17A

17B

FIG. 17. A, January 8, 1958. A thirty-four year old man. Closed fractures of the lateral malleolus and the posterior lip of the tibia. B, July 28, 1958. Six months after operation. Two posterior lip fragments were found. The lateral fragment contained the posterior tubercle of the tibia attached to the distal fragment of the fibula by the posterior lateral malleolar ligament. The medial lip fragment extended into the medial malleolus. It was necessary to expose each fragment through separate approaches in order to obtain reduction and fixation. The deltoid ligament was uninjured.

18A

18B

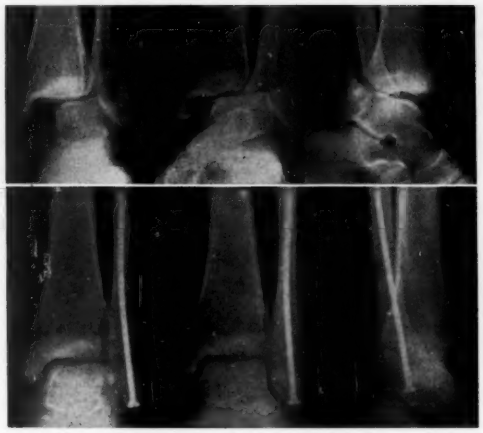


FIG. 18. A, December 30, 1958. A forty-one year old woman. Closed fractures of the lateral malleolus and lateral dislocation of the astragalus. The magnitude of the displacement suggests complete rupture of the deltoid ligament. The fracture of the posterior tubercle of the tibia indicates the posterior lateral malleolar ligament is intact. The wide displacement of the malleolar fragment from the talus indicates injury to other malleolar ligaments. B, February 4, 1959. One month after operation. The deltoid ligament was found to be completely ruptured in its middle and the posterior tibial tendon was interposed between the malleolus and the astragalus. The anterior lateral malleolar ligament was intact but the posterior lateral malleolar ligament was avulsed with the posterior tibial tubercle. Complete ruptures of the anterior talofibular and calcaneofibular ligaments were found also.

medial inferior approach. The calcaneotibial and posterior talotibial ligaments may be avulsed from either bone attachment. In this experience, tears of the mid-portion were most common. Complete tear of the talotibial ligament may permit the posterior tibial tendon to be interposed between the medial malleolus and the astragalus. (Figs. 1A through C, 18A and B.) Generally, the magnitude of maximal displacement of the astragalus will give a reasonable index to the extent of the injury to the deltoid ligament. Isolated tear of only the calcaneotibial portion of the deltoid ligament has been observed to be associated with fracture of the lateral malleolus.

Lesions of the anterior talofibular and calcaneofibular ligaments may be exposed by the lateral anterior approach. Ruptures of these ligaments commonly occur without fracture of the lateral malleolus. However, fracture of the lateral malleolus does not preclude such a possibility. (Figs. 18A and B.) Isolated major lesions of these ligaments without any associated fracture may not be discovered unless examination includes stress roentgenography with the foot in forced inversion. Isolated lesions of the posterior talofibular ligament have not been recognized. This structure may be exposed by the lateral posterior approach.

Gross lesions of both the anterior and posterior lateral malleolar ligaments are associated with dislocation of the talofibular articulation. (Figs. 10A and B, 16A and B.) Such lesions must be anticipated when fracture of the lower third of the shaft of the fibula exists even though widening of the joint space is not apparent in routine roentgenograms. Dislocation of the talofibular joint may be demonstrated by stress roentgenography. Repair of these ligaments by suture is not dependable. It is preferred to maintain reduction of the tibiofibular joint, at least temporarily, by either a bolt or a screw that traverses that joint. The selection of design of either screws or bolts for this purpose, depends in a measure on the preference of the surgeon. The standard bone screw with machine threads has been satisfactory in most cases provided it is placed transversely in the dense trabecular bone

adjacent to the distal articular surface of the tibia. (Figs. 16A and B.) When bone atrophy exists and "stripping of the threads" is feared, a slightly longer screw may be converted into a bolting apparatus by the addition of a washer and nut. Encroachment of the apparatus in the ankle joint may be avoided by determining the location of the articular surfaces by a small incision of the capsule between the anterior lateral malleolar and the anterior talofibular ligaments.

Oblique fractures of the lateral malleolus commonly extend from the proximal and posterior aspect in a distal and anterior direction. (Figs. 11A and B.) The course of the fracture line is between the anterior and posterior lateral malleolar ligaments. Displacement of the talus and the distal malleolar fragment in the lateral and transverse torsional directions may be accompanied by rupture of the posterior lateral malleolar ligament. The ligament may be ruptured in its fibrous portion (Figs. 13A and B) or may be avulsed with the posterior tibial tubercle (Figs. 17A and B). The anterior lateral malleolar ligament remains intact, being attached to the proximal malleolar fragment. Anatomical reduction and firm stabilization of the fracture of the malleolus restores the integrity of the tibiofibular articulation. Fixation of the fibula to the tibia through the tibiofibular joint then becomes unnecessary.

OPEN FRACTURES AND DISLOCATIONS

Open fractures and dislocations of the ankle joint may be caused by either direct or indirect trauma. Wounds of the skin and subcutaneous tissues resulting from indirect violence commonly have a transverse course and occur in the regions of the malleoli. Wounds of the ankle region due to direct trauma have no characteristic pattern. The management of these injuries is based upon the principles of treatment of open fractures in general. An accurate assessment of the extent and severity of injury is necessary for the proper planning of treatment. Tetanus prophylaxis is mandatory because of the likelihood of contamination by soil. General therapy with broad-spectrum antibiotics is justified by the concept of treatment of impending invasive infection, not on the basis of prophylaxis of local infection.

A meticulous and thorough wound excision accomplished soon after injury is the most dependable prophylaxis of local infection. This can be performed with greater care in a bloodless field provided by a pneumatic tourniquet about the thigh. For purposes of lavage, a small polyethelene catheter introduced into the joint cavity opposite the wound aides in the removal of tissue debris and small foreign bodies during efflux of the solution. It also hinders the introduction of bits of loosened tissue and foreign bodies into the depths of the joint during operation. The catheter may remain in the joint after operation to facilitate aspiration and the introduction of antibiotics. Because of the relative paucity of skin in the ankle region, sparing removal of only hopelessly devitalized tissue may permit wound closure without grafting.

If wound surgery has been accomplished within the first eight hours after injury, primary closure of the joint cavity is desirable. This can be accomplished in part by anatomical reduction of the fractures and dislocations. If reduction cannot be maintained, the moot question of use of internal fixation devices arises. The judicious use of standard bone screws or similar fixation apparatus may be decisive in achieving stability and aiding in closure of the joint. The approximation of edges of torn ligaments with fine, absorbable suture material helps to accomplish the goal. Injury or necessity of surgical removal may result in loss of bony or ligamentous joint structure. Closure of the joint cavity then can be accomplished only by the use of skin and subcutaneous fat. The advisability of primary closure of the remainder of the wound depends upon multiple factors. When injury has been extensive, contamination probably massive, and more than four hours have elapsed from time of injury, delay of closure for four to seven days is prudent. Such delay may be a decisive factor in the prevention of invasive infection. When primary closure of the entire wound is elected, avoidance of tension and provision for drainage of secretions are important.

Daily aspiration and bacteriological study of fluid that has collected in the joint aids in determining the efficacy of treatment. Antibiotics may be instilled into the joint, producing a more effective concentration than that obtained by the hematogenous route.

COMMENT

Some fractures and dislocations of the ankle region cannot be reduced anatomically by

closed manipulation. Interposition of soft tissue and small intermediate fragments of bone and cartilage commonly prevent closed reduction. Bosworth [2] has called attention to a type of fracture of the region of the lateral malleolus whereby the proximal fragment becomes trapped behind the posterolateral margin of the tibia and open reduction is necessary for adequate treatment. Minute fragments of bone and cartilage commonly are found loose in the ankle joint incidental to open operation.

The advocated surgical approaches provide access to all aspects of the ankle joint. Attention to anatomical details will prevent injury to major blood vessels and nerves. Unless injury exists, it is not necessary to expose the anterior and posterior tibial vessels and the tibial nerve. Superficial nerves can be avoided and preserved. Division of these nerves causes annoying areas of hypesthesia and the associated neuromas may be troublesome.

Rigid internal fixation of fractures in order to avoid additional immobilization by external means has restricted application. Only fractures with large fragments and limited comminution are amenable to this technic. The patient must be dependable. The false sense of security provided by rigid internal fixation invites weight bearing before bone healing is sound. This may lead to mechanical failure by breakage or loosening of the apparatus, to be followed by loss of reduction and delay of healing. Small fragments do not permit the insertion of sufficient apparatus to neutralize stresses of active movements through physiological ranges before additional support is provided at least by partial healing. Recently sutured ligaments have relatively little strength and they cannot be expected to lend stability.

The extent and duration of external immobilization with plaster depends in a measure on the severity of the injury. The healing of noncomminuted fractures and repaired ligamentous tears generally is advanced sufficiently in four to eight weeks so that the extremity may be removed from plaster for guarded active motions three or four times daily for short periods. The time of initiating weight bearing depends upon the re-establishment of bony continuity. When comminution has not been severe, this may be started six or twelve weeks after operation. Severe comminution may delay healing to such a point that weight bearing must be deferred for six months or even longer.

Wound infection is the most serious postoperative complication. Although its complete avoidance cannot be expected, certain safeguards must be observed in order to minimize its incidence. The condition of the skin prior to operation must be scrupulous. Blebs, abrasions of more than four hours' duration, cutaneous infections, and severe swelling are contraindications to immediate operative treatment. The most careful attention must be given to aseptic technic. If oozing cannot be controlled completely at the time of operation, provision should be made for drainage of blood and serum from the wound during the first few days afterward. Local or general antibiotic therapy cannot be expected to prevent local infection. Marginal wound necrosis occurs when there is swelling and closure has been made with excessive tension. Loss of reduction may be prevented by the adequate use of fixation apparatus, both internally and externally. Delay of bony healing can be expected when the blood supply to fragments has been interrupted, approximation is inaccurate and immobilization is inadequate.

The most disabling sequela of fracture or dislocation about the ankle is post-traumatic arthritis. Anatomical restoration of the part is the most important contribution the surgeon can make to its prevention. The severity of the injury may be a determining factor which cannot be controlled. In this regard, Cox and Laxson [6] have written, "It must be remembered, however, very definitely, that trauma severe enough to cause bimalleolar fracture-dislocation of any degree can effectively cause damage to the subchondral bone of the tibia or to the astragalus sufficient to interfere grossly with the nutrition to the articular cartilage of the ankle and lead to osteoarthritis which will develop within one to two years." Prolonged delay in treatment and prolonged external immobilization are other factors that contribute to joint stiffness.

Persistent soft tissue swelling of the foot and leg may be controlled by the use of semirigid dressings such as a modification of the Unna boot. It has been observed among thirty-five patients whom I have treated in the past ten years that those with severe injuries were more likely to have chronic soft tissue swelling about the ankle in spite of adequate open reduction than those who had less severe injury.

Symptomatic adventitious bursae are likely

to develop over fixation apparatus that is superficial. Because of the paucity of subcutaneous tissue in the region of the ankle, such bursae are likely to develop. The only reliable treatment is removal of the apparatus as soon as it has fulfilled its purpose. The direction and magnitude of movements of the tibiofibular articulation are not known completely [*4*]. Where ordinary bone screws or bolts transverse the tibiofibular joint, loosening or breakage is likely to occur if bony arthrodesis does not take place spontaneously. Therefore, patients who have such treatment are advised to have the apparatus removed after healing is complete since it is likely to cause irritation and symptoms. Not all agree with this advice [*15*].

SUMMARY

If anatomical reduction of closed fractures and dislocations of the ankle region of the adult cannot be achieved and maintained by closed technics, open reduction and fixation by a combination of internal and external means may delay the onset of disabling symptoms of post-traumatic arthritis. A concise and practicable classification of these osseoligamentous injuries is difficult because of the variety of combinations. A basic understanding of the functional anatomy of the ankle region coupled with careful physical and roentgenographic examinations permit correlation of the direction and magnitude of maximal spatial displacement of the astragalus in reference to the tibia with the extent and type of osseoligamentous injury. Accurate preoperative diagnosis is essential in order to plan surgical approaches and methods of fixation. Five basic paramelleolar approaches provide access to all aspects of the ankle joint and serve adequately for open reduction and internal fixation of the major proportion of closed fractures and dislocations. Attention to anatomical details prevents injury to major vessels and nerves. A thorough knowledge of the general principles of internal fixation of fractures and meticulous attention to details of technic are of greater importance in rendering successful treatment than the use of elaborate fixation apparatus. Technics of internal fixation of common fractures and repair of ligamentous lesions are discussed and illustrated. Some complications can be avoided by awaiting restoration of bony continuity and sound ligamentous healing before unsupported weight bearing is initiated. Factors other than anatomical restoration have significant influence in the prevention of certain sequelae, such as symptomatic postraumatic arthritis. Open reduction is hazardous and should be reserved for those patients in whom more conservative measures are likely to fail.

Acknowledgment: I wish to express my appreciation to Miss Kay Hyde who made the drawings and to Mr. Henry Raphael, Jr. who took the photographs.

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DISCUSSION

Francis J. Cox (San Francisco, Calif.): In 1951 we reviewed 213 cases of fracture of the ankle joint

in which patients were observed and followed up to their end point of recovery on the Stanford Service of the San Francisco Hospital. We reported on these cases at that time. We have no quarrel with anything that Doctor Jergesen has said today; as a matter of fact we are in complete agreement with every detail. There may be some minor differences in the extent of internal fixation utilized, but the fundamental issue at hand, namely, accuracy of reduction as a major aim is accepted. The method of achievement of this ultimate objective is a minor issue.

Since we are addressing to a major degree a group of general surgeons, some of whom are interested in fractures and traumatic surgery, I think, rather than discuss the specific points made by Doctor Jergesen, it would be wise to expand on a few areas which he did not touch upon in his paper.

Sometimes, when there is a minor fracture of the medial side of the ankle, it is wiser to center attention on the soft tissue problem; for example, the tiny spiral fragments of the tip end of the medial malleolus which truly represent a disruption of the medial collateral ligament. This is the more serious problem, not the small bony fragment. If the fragment is excised, and it should be, then the ligament must be repaired anatomically according to the methods outlined by Doctor Jergesen. In this fashion the ankle becomes completely stable again. Operative repair of the ligament is the essential part of the procedure. Simple excision of the small fragment of bone is not sufficient.

There are a few injuries to the ankle that should never be treated surgically. The major example of this is the epiphyseal fracture of the distal end of the tibia that occurs commonly in children, which many people refer to as a "broken ankle" in the child. No matter how gently these may be managed, no matter what care may be exercised, a certain number of these injuries will develop catastrophic end results with a loss of growth and gross distortion of the weight-bearing alignment of the limb, the ankle and the foot. The most unfortunate fact about the end result of this type is that it can never be surgically corrected satisfactorily. If this be true, and it is, then any surgical approach (even violence of manipulation) upon the original fracture is totally wrong and must be avoided at all times. Any interference that might lead to establish a true arrest of growth of the distal tibial epiphyseal plate is to be condemned. To a group of general surgeons, a recent experience of an epiphyseal injury in a child might prove interesting. The lesson to be learned is equally applicable to injuries to the ankle, although the injury in question here occurred through the proximal tibial epiphysis.

This youngster was struck by a car and sustained an epiphyseal fracture of the proximal tibia with complete severance of the popliteal artery and vein. These major vessels were repaired by primary end-to-end anastomosis and the fracture was reduced. Six weeks later an arteriogram was performed for informational purposes.

The major vessels, as might be expected, were completely occluded and the circulation to the limb below was passing through the geniculate vessels entirely. A point of interest was noted in the appearance of an extremely heavy deposit of dye in the end arteries of the bone immediately adjacent to the epiphyseal plate. The dye did not appear in that portion of the bone where the epiphyseal plate had been torn free. One might interpret an arteriogram such as this as showing an early indication of arrested growth. Clinical evidence would lead one to believe that such is not the case. However, very few injuries of this type, certainly less than 5 per cent, develop an arrested growth except after operative intervention.

It would be interesting if more arteriographic studies were made following injuries of this type, namely, epiphyseal disruption due to trauma. There is very little actually that we know as to how the circulation re-establishes itself and how growth proceeds following an injury to this region. Cooperative interest between the surgeon who treats fractures and the vascular surgeon might lead to some worthwhile information along these lines.

I think it would be worth while to re-emphasize a point made by Doctor Jergesen, namely, that even though absolutely accurate anatomical reduction of the fracture dislocation of the ankle can be achieved surgically, there is no reason, however, to believe that you can still avoid development of a serious degenerative osteoarthritis. This may be the result of the total damage incurred at the date of original injury and therefore may be totally inevitable. A guarded prognosis for a complete recovery and a painless weight-bearing extremity should be undertaken in every case of serious fracture dislocation.

Finally, I think it is worth while to point out that the incidence of a reflex sympathetic dystrophy following minor or major injuries to the ankle joint is quite common. The classical findings of a stiff rigid foot produced by Sudeck's atrophy must be aborted and never allowed to develop. This can only be accomplished by an awareness of the condition, early diagnosis and prompt early treatment with local anaesthetic agents, i.e., cortisone derivitives, sympathetic blocks or even in a few rare instances by sympathectomy.

I have enjoyed Doctor Jergesen's paper and again can find no area of disagreement with anything that he has said.

The Routine Culture of Surgical Wounds*

FREDERIC P. SHIDLER, M.D., *Menlo Park, California*

THIS is a study of cultures taken from contaminated wounds after injury and from surgical incisions just prior to closure of the skin in order to determine, first, if bacteria could be found, and second, whether wound infections would develop when bacteria were recovered from surgical wounds.

Swabs taken from the serum of the subcutaneous fat were dropped directly into sterile test tubes containing thioglycollate culture broth. Cultures showing bacterial growth were streaked upon blood agar plates from which the bacteria were identified.

ACUTE TRAUMATIC WOUNDS

In 1953 the study began with traumatic wounds in ambulatory patients treated in the office. Since many surgeons at that time routinely administered antibiotics to patients with grossly contaminated and contused wounds, we speculated whether wound cultures would demonstrate viable organisms against which antibiotics should be directed.

A simple but meticulous technic was employed in all cases. This consisted of careful scrubbing of the wound edges and adjacent skin area for several inches in all directions with pHisoHex® and water. No other skin cleansing or cleansing agent was employed. The wounds were anesthetized with 1 per cent procaine injected through the gaping wound into the surrounding tissues. Skin edges and all grossly non-viable subcutaneous tissues or tissues with imbedded dirt particles were carefully excised. Following excision and hemostasis, the wounds were irrigated by a sterile bulb syringe with sterile normal saline in copious amounts. Swabs of the depths of the wound were dropped directly into thioglycollate culture media. The wounds were then sutured without drainage. Wounds of the extremities and digits were splinted in plaster of paris or small metal supports.

The surgeon wore no mask or sterile gown. He donned sterile gloves without a preceding standard surgical scrub. Either of the same two surgeons treated all of these wounds.

From the first twenty patients thus treated, there were sixteen sterile wound cultures. No antibiotics were given and all wounds healed per primam. They are briefly described:

1. 3.5 cm. laceration of thumb into pulp of distal phalanx
2. 9 cm. laceration of back
3. 12 cm. laceration of left ankle
4. Contused ragged laceration of tip of middle finger
5. Ragged laceration and avulsion of tip of little finger
6. Deep laceration of lower leg
7. 6 cm. laceration of posterior thigh through subcutaneous fat to muscle
8. 4 cm. laceration of left wrist exposing ulnar artery and dividing flexor carpi ulnaris
9. 5 cm. laceration of right anterior axillary fold through subcutaneous fat, partially dividing portion of pectoral muscle
10. 7 cm. laceration of left arm exposing biceps muscle, and 7 cm. laceration of left forearm exposing extensor carpi radialis and periosteum of ulna in a flap-type laceration
11. 2.5 cm. laceration of right forearm with imbedded BB shot
12. 5 cm. gaping laceration in thenar eminence of left thumb, dividing flexor pollicis brevis and containing grass and dirt
13. Laceration of left ankle and foot
14. 2.25 by .75 cm. avulsion of skin of phalanx of left thumb; Wolff graft
15. 2 cm. laceration of dorsum of hand
16. 5 cm. laceration of forehead.

The four remaining patients had positive wound cultures. Two were Staphylococcus

* This study was supported by the Medical Research Foundation for Palo Alto Hospital.

albus. The first patient had a curving laceration of the eyelid across its margin. The wound healed per primam without administration of antibiotics. The second patient sustained a crushing contused laceration of the terminal phalanx of the thumb with a compound fracture. A portion of the bone was removed and the wound was sutured. Mild wound infection developed but was controlled with erythromycin to which this particular Staph. albus infection was sensitive. The wound healed without osteomyelitis. The third patient had a laceration of the chin from which staphylococcus and gram-negative rods were cultured. It healed after mild infection without antibiotics. The fourth patient had a V-shaped laceration into the axilla from which Staph. aureus was recovered. The organism was sensitive to penicillin and the wound healed per primam after three daily doses of long-acting penicillin injected intramuscularly.

On the basis of these findings, the same technic was employed for the next thirty-one patients who required suture of lacerations in the office. All wounds healed per primam without the use of antibiotics.

HOSPITAL SURGICAL WOUNDS

The Palo Alto Hospital has 251 beds exclusive of delivery rooms, maternity and newborn nursery wards. In 1957 6,334 operations and in 1958 6,696 operations were performed in four major and two minor operating rooms.

All surgeons scrubbed preoperatively with pHisoHex, and wore caps, sterile masks, gowns and gloves. The skin preparation for the operative field consisted of a scrub with pHisoHex and water, to which certain surgeons added tincture of Zephiran® or aqueous Zephiran, 1:1000. After the fascial layers of the wounds had been closed, cultures were obtained by simple swab method from the subcutaneous fat, transferring the swab to thioglycollate broth immediately.

From March 24, 1958 through July 31, 1958, wound cultures were obtained from 546 operations of a total of approximately 2,200 operations performed by forty different surgeons. The majority were elective surgical procedures. There were 134 positive cultures.

In Table 1 are listed the types and number of operations from which cultures (positive and sterile) were obtained.

TABLE 1
TYPE AND NUMBER OF PROCEDURES OF 546 OPERATIONS STUDIED; 134 POSITIVE CULTURES

Type of Procedure	No. of Operations	
	Positive Cultures	Sterile Cultures
General surgery:		
Inguinal and femoral hernioplasty	75	.....
Incarcerated inguinal or femoral hernioplasty	3	.....
Repair of epigastric hernia	3	.....
Repair of umbilical hernia, bilateral vein stripping	..	1
Repair of incisional hernia	..	3
Correction of omphalocele	1	.....
Appendectomy	32	.....
Removal of perforated appendix	1	.....
Cholecystectomy	30	.....
Cholecystoduodenostomy	..	1
Exploration of common bile duct	2	.....
Gastric resection	17	.....
Gastroenterostomy	3	.....
Vagotomy, pyloroplasty or gastroenterostomy	..	4
Perforated duodenal ulcer	3	.....
Repair of esophageal hiatus hernia, transabdominal	..	3
Repair of esophageal hiatus hernia, transthoracic	..	4
Fredet-Ramstedt pyloromyotomy	..	2
Splenectomy	..	1
Correction of bowel obstruction	4	.....
Correction of intussusception	..	1
Resection of bowel	3	.....
Resection of colon	8	.....
Colotomy for removal of polyps	5	.....
Colonic transplant (ascending) to cervical esophagus	1	.....
Revision of colostomy	1	.....
Closure of colostomy	..	1
Abdominoperineal resection	1	.....
Exploratory laparotomy	8	.....
Exploratory laparotomy, removal of cyst on kidney	1	.....
Thyroidectomy	15	.....
Removal of cyst of thyroglossal duct	2	.....
Biopsy of breast	11	.....
Radical mastectomy	3	.....
Removal of breast abscess	1	.....
Vein stripping	6	.....
Ligation of veins	..	2
Amputation of thumb and dissection of axillary node	1	.....

TABLE 1 (*Continued*)
TYPE AND NUMBER OF PROCEDURES OF 546 OPERATIONS STUDIED; 134 POSITIVE CULTURES

Type of Procedure	No. of Operations: Positive Cultures	No. of Operations: Sterile Cultures
Dissection of aortic node	..	1
Biopsy of lymph node	..	1
Excision of subcutaneous lipomas	..	2
Excision of skin tumor	1	.....
Excision of skin tumor	..	2
Plastic surgery on hand	..	1
Excision of salivary gland	..	2
Excision of tumor on buttock	..	1
Secondary closure of abdominal wound	..	1
Insertion of aortic graft	..	1
Lumbar sympathectomy	..	2
Excision of pilonidal sinus	8	.....
Gynecology-cesarean section:		
Cesarean section	23	.....
Cesarean section plus tubal ligation	..	7
Cesarean section plus hysterectomy	..	1
Tubal ligation, postpartum	..	8
Abdominal hysterectomy	49	.....
Vaginal hysterectomy	3	.....
Vaginal repair	1	.....
Plastic surgery on fallopian tubes	1	.....
Pelvic laparotomy (excision of endometrial implants, ovaries, uteri)	28	.....
Oophorectomy	3	.....
Excision for ectopic pregnancy	..	1
Thoracic surgery:		
Transthoracic sympathectomy	..	1
Pericardiectomy	..	1
Pulmonary segmental lobectomy	..	2
Exploratory thoracotomy	6	.....
Ophthalmology-otolaryngology:		
Correction of strabismus	1	.....
Otoplasty	..	1
Removal of cataract	..	1
Neurosurgery:		
Craniotomy	4	.....
Laminectomy, sometimes with spinal fusion	27	.....
Musculo-tendon-skeletal surgery:		
Arthrotomy of knee	14	.....

TABLE 1 (*Continued*)
TYPE AND NUMBER OF PROCEDURES OF 546 OPERATIONS STUDIED; 134 POSITIVE CULTURES

Type of Procedure	No. of Operations: Positive Cultures	No. of Operations: Sterile Cultures
Patellar transplant	..	15
Revision amputation of leg	1	.....
Hip nailing, hip prosthesis	5	.....
Amputation of leg	..	1
Osteotomy (open reductions, plates, screws)	..	15
Excision of exostosis	..	1
Insertion of bone graft	..	1
Removal of bone screw	4	.....
Spinal fusion	..	1
Bunionectomy	..	4
Excision of ganglion	..	1
Excision of bursa	1	.....
Excision of coccyx	1	.....
Correction of hammer toe	..	1
Scalenotomy	..	1
Repair of tendon	..	5
Suture of traumatic laceration	..	2
Urological surgery:		
Exploration of kidney	6	.....
Ureteral exploration	4	.....
Segmental resection of bladder	..	1
Retropubic prostatectomy	2	.....
Hydrocelectomy	..	1
Orchiopexy	1	.....
Orchiectomy for torsion of testis	..	1
Ventriculonephrostomy	..	1

Table 11 shows the details of the 134 positive wound cultures: the type of organism, the type of operation and the number of operations from which it was recovered, and whether antibiotics were administered postoperatively. Forty-six patients received antibiotics postoperatively, and eighty-eight patients received none. Staph. aureus was coagulase-positive. Staph. albus and citreus were coagulase-negative.

The asterisk symbol (*) designates the five patients with wound infections. Two of these gave cultures of alpha hemolytic streptococcus. Three gave cultures of Escherichia coli. Five hundred forty-one patients had no wound infection.

TABLE II

TYPE AND NUMBER OF OPERATIONS, WITH ANTIBIOTICS OR NO ANTIBIOTICS GIVEN POSTOPERATIVELY; 134 POSITIVE WOUND CULTURES

Organism	Antibiotics		No Antibiotics	
	Operation	No. of Cases	Operation	No. of Cases
Hemolytic Staph. aureus	Cesarean section	1	Ocular muscle cinch	1
Non-hemolytic Staph. aureus		..	Inguinal hernioplasty (unilateral)	1
Hemolytic Staph. albus	Gastric resection	1	Inguinal hernioplasty (unilateral)	5
	Cholecystectomy	2	Inguinal hernioplasty (bilateral)	3
	Correction of bowel obstruction, lysis of adhesions	2	Femoral hernioplasty (bilateral)	1
			Epigastric hernioplasty	1
	Open colonic anastomosis	1	Cholecystectomy	4
	Colotomy for removal of polyp	1	Gastric resection	2
	Right colon transplant to neck	1	Resection of bowel	1
	Hysterectomy	3	Hysterectomy	5
	Pelvic laparotomy	1	Ovarian cystectomy	2
	Simple mastectomy	1	Cesarean section	3
	Laminectomy	2	Appendectomy	2
			Radical mastectomy	2
			Simple mastectomy	1
			Removal of breast abscess (drained)	1
			Thyroidectomy	2
			Bilateral vein stripping	1
			Laminectomy	1
			Lumbar sympathectomy	1
			Resection of urinary bladder (drained)	1
			Orchiopexy	1
			Excision of pilonidal cyst	3
			Retropubic prostatectomy	1
			Revision amputation	1
Non-hemolytic Staph. albus	Hysterectomy	1	Inguinal hernioplasty (unilateral)	3
	Abdominoperineal resection	1	Inguinal hernioplasty (bilateral)	4
	Removal of cyst on kidney	1	Appendectomy	2
	Vein stripping	1	Exploratory laparotomy, removal of cyst on kidney	1
	Amputation of thumb, axillary dissection	1		
			Hysterectomy	1
	Craniotomy	1	Cesarean section	2
			Plastic surgery on fallopian tube	1
			Ligation of fallopian tube	2
			Excision of ovarian cyst	1
			Biopsy of breast	2
			Simple mastectomy	1
			Vein stripping, bilateral	1
			Excision of thyroglossal cyst	1
			Arthrotomy of knee	1
			Excision of olecranon bursa	1
			Removal of intramedullary pin	1
			Coccygectomy	1
Staph. citreus		..	Inguinal hernioplasty (unilateral)	1
Alpha hemolytic streptococcus	Vaginal hysterectomy	1	Inguinal hernioplasty (unilateral)	1
	Closure of perforated duodenal ulcer*	2	Appendectomy	1
			Resection of colon	1
	Excision of large nevus*	1	Cesarean section, appendectomy	1

TABLE II (*Continued*)

TYPE AND NUMBER OF OPERATIONS, WITH ANTIBIOTICS OR NO ANTIBIOTICS GIVEN POSTOPERATIVELY; 134 POSITIVE WOUND CULTURES

Organism	Antibiotics		No Antibiotics	
	Operation	No. of Cases	Operation	No. of Cases
Non-hemolytic streptococcus	Gastrotomy	1	Appendectomy	1
	Vaginal hysterectomy	1	Open reduction with nailing (femoral head)	1
Proteus	.....	..	Resection of bowel	1
			Vaginal repair	1
Diphtheroids	Appendectomy	1	Laminectomy	1
	Revision of gastric resection, partial pancreatectomy	1	Arthrotomy of knee	1
			Vein stripping (bilateral)	1
	Exploration of common biliary duct	1	Excision of pilonidal cyst	1
			Cholecystectomy	1
Pseudomonas aeruginosa	Thoracotomy, excision of pulmonary bleb	1	.....	..
Bacillus subtilis	Cholecystectomy (acute)	1	Closure of omphalocele	1
	Pulmonary lobectomy	1		
	Ureterectomy	1		
E. coli	Appendectomy	3	Inguinal hernioplasty (bilateral)	1
	Cholecystectomy	1		
	Resection of colon	1		
	Revision colostomy*	1		
	Colotomy for removal of polyp*	1		
	Hysterectomy	1		
	Correction of bowel obstruction, spill of small bowel contents*	1		
	Bilateral inguinal hernioplasty and hydrocelectomy	1		
	Vein stripping, unilateral (varicose ulcer)	1		
Total: All operations	.....	46	.....	88

* Wound infection.

COMMENTS

Acute Traumatic Wounds. The experience with acute traumatic wounds leads to the following observations. First, culture of acute traumatic wounds after excision and irrigation with normal saline prior to closure by suture provides an accurate means of predicting bacterial growth in the wound. Second, within forty-eight hours an organism can be identified from a positive wound culture and its sensitivity to antimicrobial agents determined. Third, lacerations which are treated as mentioned with procaine anesthetic will usually be sterile or will contain non-pathogenic bacteria, and will usually heal without any antibiotic administration. Fourth, the well established principle of careful excision of contused skin edges, grossly traumatized non-viable tissue and foreign bodies, followed by copious irrigation with sterile normal saline, yields a high percentage of healing per primam. Fifth, procaine infiltration of adjacent tissue through the acute, gaping, post-traumatic wound does not increase the incidence of wound infection.

Hospital Surgical Wounds. The five postoperative wound infections occurred in patients who had positive cultures from the surgical wound at its closure, and the identical organism was found in the discharge from the infection in the postoperative period. Only pathogenic organisms produced wound infections. Three of these yielded E. coli from the surgical wound at the time of operation and from the drainage of the infected wound at a later date. The one serious infection followed colotomy and removal of a benign polyp. Infection of the entire wound developed, followed by evisceration. In the second patient a localized infection developed in the lower midline wound through which a mechanical obstruction of the small intestine had been relieved and in which small bowel contents had been inadvertently spilled. Healing occurred after drainage through the operative scar. In the third patient a self-limited abscess developed following colostomy revision. Prompt healing occurred after drainage of the abscess.

Alpha hemolytic streptococcus was cultured from the surgical wound and from the wound infection of the remaining two patients. One of these infections occurred after excision of an extensive skin nevus and required removal of all sutures to heal by granulation. The other was in an abdominal wound following closure of a perforated duodenal ulcer. This wound had a ocalized infection which healed after the removal of one or two cotton sutures from the linea alba.

Four of the five wound infections followed open operations on the intestinal tract: a perforated duodenal ulcer (alpha streptococcus), bowel obstruction in which intestinal contents of the obstructed small bowel had been spilled (E. coli), colotomy for polyp removal (E. coli), and colostomy revision (E. coli). Neither the patient with the perforated ulcer nor the patient with the small bowel obstruction had received intestinal or intramuscular antibiotics before operation, and both had a considerable volume of intestinal content exposed to the wound. Both patients upon whom colonic operations had been performed had been prepared with oral intestinal antibiotics, but both had viable E. coli bacilli at the time of operation. All four patients received postoperative antibiotics in standard dosage, but wound infections developed in all.

Review of the twelve patients from whose wounds were cultured E. coli (Table II) shows that the nine patients who had no wound infections also did not have a large quantity of intestinal content exposed to the wound, but eight patients received prophylactic antibiotics. In fact, five of these operations did not concern the intestinal tract at all. Hence it is suggested that a quantitative relationship exists between E. coli bacterial inoculum and later wound infection.

Staph. aureus, coagulase-positive, was cultured from three different patients of the 134 with positive cultures. Wound infections did not develop in any but one received prophylactic antibiotics.

Staph. albus, coagulase-negative, was the most frequently recovered organism, and was found in ninety-one patients. Wound infections did not develop in any although twenty-one received prophylactic antibiotics.

There were ninety-five editorially classified different types of operations of the 546 operations studied. In forty-six of these categories there were sterile wound cultures, but only four of these categories contained more than five operations. They were: seven cesarean sections with tubal ligations; eight tubal ligations, postpartum; fifteen patellar transplants; and fifteen osteotomies.

The schedules of operations were scrutinized to see if positive wound cultures could be related to the surgeon, the scrub nurse, the anesthetist, the location of the operating room or the time of day. No correlation was established.

CONCLUSIONS

This study of both acute traumatic and elective surgical wounds strongly suggests that bacteria which are present at the time of wound closure are the origin of surgical wound infection. Furthermore, bacteria in surgical wounds may be detected at the time of suture and identified by means of culture prior to the development of clinical infection.

Convincing bacteriologic evidence is offered in support of meticulous wound excision followed by copious irrigation with normal saline solution in the treatment of acute traumatic wounds. Sixteen of twenty such patients had sterile wound cultures.

Routine wound culture taken in the operating room provides a fairly simple, useful means of assessing the bacterial population in surgical wounds at the time of operation.

Approximately 25 per cent of patients operated upon at this hospital showed bacteria in their surgical wounds. Most of the bacteria identified were non-pathogenic. No wound infections followed cultures positive for non-pathogenic organisms. Their presence may indicate a minimum beyond which skin cleansing agents cannot be effective in sterilization. or their presence may raise the question of correctable errors in aseptic technic by operating room personnel.

These data speak strongly against the routine use of antibiotics as prophylaxis for wound infection in surgical patients. There is striking evidence that non-pathogenic organisms will not produce wound infections and, hence, antibiotics are needless. Not all wounds which harbored pathogenic organisms developed wound infection, but pathogens were found in all wound infections. Antibiotics failed to prevent infection in the five cases observed, but no doubt the antibacterial agents modified the course of the infection in all but one patient.

Effective antibacterial therapy in surgical patients should follow the reasonable steps of first identifying a pathogenic organism by culture, then testing its sensitivity to antibacterial agents, followed by the administration of the drug most effective against the organism. Such a therapeutic plan may not prevent a wound infection but it may control infection elsewhere, such as in pleural or peritoneal cavities.

SUMMARY

1. Cultures from acute post-traumatic lacerations were taken after wound excision and irrigation in twenty successive patients. Sixteen of these were sterile cultures. Two mild infections developed in association with the four positive cultures.

2. Cultures were obtained from the wounds of 546 patients undergoing surgery in the hospital operating room. One hundred thirty-four positive cultures were obtained. Ninety-seven of the positive cultures were Staph. albus.

3. Five wound infections occurred in the 134 positive cultures from hospital patients. Three of these cultured E. coli, and two cultured alpha hemolytic streptococcus. The identical organism was found in the surgical wound at the time of closure, and in the drainage of the subsequent wound infection.

4. Bacteria present in the surgical wound at the time of closure are the origin of wound infections.

5. Antibiotics will not prevent wound infections in surgical patients but meticulous aseptic surgical technic will.

DISCUSSION

H. Rocke Robertson (Vancouver, B. C.): I have been impressed by two things in particular in Dr. Shidler's report. First is the fact that he carried out such an extensive program of research in his own office. Too often, I think, we fail to realize that a wealth of material passes through our offices, and we neglect the opportunity these cases give us for making useful observations. Dr. Shidler, rather like Lord Lister in this regard, took advantage of his office patients and went to no end of trouble to make cultures, transport them to the hospital lab and so on, and I think he deserves a great deal of credit for this. The second thing that impressed me was the low incidence of infection in both the traumatic cases and, more important, in the elective cases, for his rate of frank wound infection in a sizeable series of cases of a wide variety was well under 1 per cent which is an excellent record. He makes the point that wound infection probably arises from organisms present in the wound at the time of closure, that is, that they do not often arise from organisms introduced after the wound is closed or delivered to the wound by the blood stream. I agree with this conclusion. The only exception I would make is that I think occasionally wound infection arises from the region of drains.

The organisms he has discovered in the wound that have eventually caused infection may have come from dust in the air, from the surgeon's or the assistant's hands or noses, or from the patient's own skin. All these sources are important and there is no question that all, from time to time, are the vehicles of the organism. However, I would like to confine my attention to the patient's skin as a source of his own wound infection, a possibility that we have been exploring lately on the thesis that it is always nice to be able to blame someone else and that if it is the patient who can be blamed at times, the surgeon may be relieved by having someone with whom to share the responsibility. I have two observations to make. The first is along the lines of Dr. Shidler's, namely, that the incidence of wound infection in patients with pathogens on their skin preoperatively is five times greater than in patients without pathogens. This figure was obtained by swabbing the skin of a large number of patients at the site of operation at the time of admission and then following up these patients through their stay in the hospital. When pathogens were found on the skin surface at the time of admission to the hospital,

the likelihood of infection of the wound caused by those same pathogens, in this instance, staphylococci, was five times as great as when no pathogens were found. Second, bearing on this same point, there was a reduction in the incidence of infection on our surgical service following the introduction of a painstaking skin preparation. The incidence of wound infection on our general surgical service at the Veterans Hospital over a three-year period has dropped in the last six months due, I think, to the addition of a particularly careful skin preparation prior to the operation, eliminating the patient's skin factor as much as possible.

FREDERIC P. SHIDLER (closing): If one surveys the twelve organisms listed in Table II of my paper, in view of Dr. Robertson's last point, I think one will be impressed by the fact that these twelve organisms are the normal inhabitants of the skin; certainly Staph. aureus is a common one. This may mean that more attention to the preparation of the skin is needed, or it may mean that this is as clean as we can get the skin.

Technic and Indications for Miller-Abbott Tube Intubation

A RAPID METHOD OF INTRODUCTION

RALPH H. LOE, M.D., *Seattle, Washington,* AND C. E. M. TUOHY, JR., M.D., *Snohomish, Washington*

THE use of the Miller-Abbott tube in intestinal obstruction as introduced by Abbott and Johnston in 1938 [*1,2*] marked an important milestone in the management of this hitherto highly lethal disease. At Presbyterian Hospital in New York [*3*] the mortality rate for this condition in the years immediately prior to the introduction of intubation was 29.6 per cent and was reduced to 5.9 per cent after the introduction of the Miller-Abbott tube. In 1939 the senior author learned Abbott's technic of intubation which utilized a wire stylet to facilitate passage of the tube into the duodenum. However, successful introduction was difficult and often required twenty-four hours. Failures were not infrequent. As a result many other tubes [*4–7*] were developed but the modifications were either difficult to use, expensive or not generally available [*8,9*] in the average hospital stockroom. A single-lumen tube with mercury, as introduced by Harris [*10*] and also by Cantor [*11*], did have some advantage in ease of passage and better suction but progress down the small intestine was slower and less satisfactory than with the air-inflated balloon.

While the use of these tubes was considered a valuable adjunct in the management of small bowel obstruction, the devilish difficulties of introduction in the obstructed patient resulted in many surgeons abandoning their use for intestinal suction.

It is the purpose of this paper to present a simple method of intubation which combines the gravity effect of mercury in the balloon and a wire stylet to give the tube sufficient rigidity to force its passage through the pylorus. With this combination of older methods we have been able to pass the Miller-Abbott tube into the duodenum in a matter of minutes instead of hours.

It is preferable to pass the tube in the patient's room. The time spent in the x-ray department is then cut to the minimum as the balloon is usually at the pylorus, if directions have been carefully followed.

The equipment needed includes: a Miller-Abbott tube, No. 60 to 70 pound self-straightening leader wire, 2 per cent Pontocaine® with Adrenalin,® a 50 cc. syringe, 5 cc. of mercury, split BB shot, wire pliers, K-Y® jelly and mineral oil.

The introduction and passage of the Miller-Abbott tube is accomplished in the following manner.

IN THE PATIENT'S ROOM

1. The balloon is filled with air and tested for leaks under water. The capacity of the balloon is measured.

2. The more open nostril of the patient is swabbed or sprayed with 2 per cent Pontocaine and Adrenalin solution.

3. A 36 inch length of No. 60 to 70 pound leader wire is lubricated by passing it through a soft, wet bar of soap.

4. A wire is introduced through the metal end of the Miller-Abbott tube and directed up the suction lumen until only 3 inches remain outside the tip. By gently bending the tubing back and forth over the end of the wire an area of single-thickness tubing can be determined. The wire is then made to puncture the tubing thus avoiding injury to the balloon side of the tube. (Fig. 1.)

5. The wire is drawn upward until the distal tip is directly beneath the wrapping at the proximal margin of the balloon. The wire is then

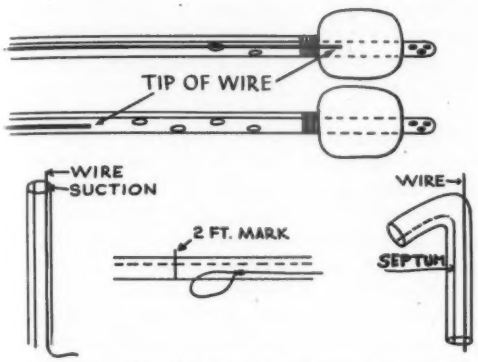

FIG. 1. Technic of wire introduction. Top, the preferred position of the wire stylet. Lower right, the method of perforating the rubber tube, avoiding damage to the septum.

marked at its exit from the tube by clamping on a split BB, thus fixing its intraluminal position. The remaining wire is bent in the shape of a ring or clamped with a hemostat.

6. Mercury, 3 cc., is injected into the balloon.

7. With the balloon lubricated and the patient's neck flexed, the tip is introduced into the nose. When it reaches the pharynx the head is thrown backward. This allows the mercury to carry the tube down the throat, and with a swallow of water it is easily propelled into the stomach.

8. The balloon is distended with air and pulled out until it is stopped by the cardio-esophageal sphincter. This should bring the tube to its one-ring marking and serves to check accuracy of the tube markings. The two-ring mark indicates the pylorus and the three-ring mark the ampulla of Vater. (Fig. 2.)

9. The stomach is emptied and 300 cc. of air is injected. This will overcome any spasm of the antrum which might prevent the tube from reaching the pylorus. The balloon is deflated.

10. The patient is now turned well over on his right side. (Fig. 3.) In this position, with the patient taking sips of water, 6 to 9 inches of tubing is gradually fed into the stomach. Thus the weight of the mercury carries the tip of the tube to the pylorus following along the anterior wall of the stomach and avoiding the otherwise obstructing spinal column. (Fig. 3.)

The air is removed from the stomach, the tube is anchored to the nose, and the patient is placed on his back and taken to the fluoroscopy room.

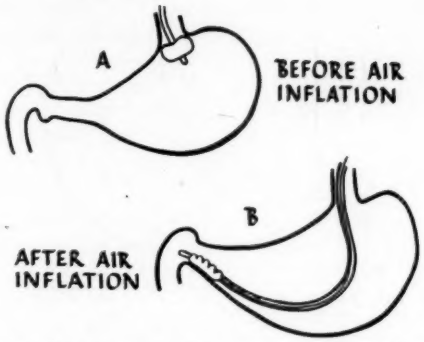

FIG. 2. A, the antrum of the stomach contracted before air inflation. B, after inflating the stomach with air, antral spasm is overcome.

IN THE FLUOROSCOPY ROOM

1. The tip of the tube in most instances will be seen at the pylorus. If it is not, further manipulation following the previously described technic will be necessary under the fluoroscope. The addition of 2 to 3 cc. of mercury to the bag may be of assistance.

The patient is turned on his right side and moderate pressure is exerted on the tip of the tube by means of the stylet. The tube usually passes through the pylorus in one to fifteen minutes. A swallow or two of water may help. In exceptional cases nitroglycerin administered sublingually or the injection of atropine may relax the sphincter. If the stomach is J-shaped, tilting the head of the fluoroscopic table downward should be tried. The addition of 3 to 4 cc. of mercury in the balloon may give enough weight to force passage.

2. The tube, having passed the pylorus, is easily advanced to the lower third of the second

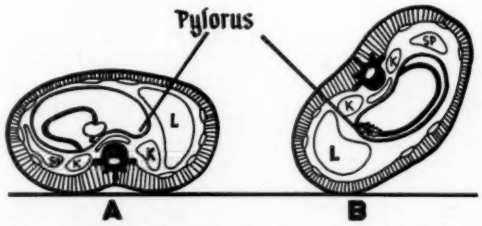

FIG. 3. Use of body position and gravity in intubation. A, the obstructing influence of the spine and the tendency for the tube to coil in the fundus with the patient lying on his back. B, in this position the weighted tip of the tube avoids the spinal column and follows the anterior wall of the stomach to the pylorus.

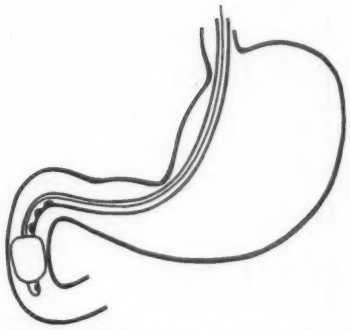

FIG. 4. Position of the tube at the time of wire removal. Mineral oil is injected in the suction portion of the tube, thus facilitating withdrawal of the wire. The position of the tip is then verified under the fluoroscope and the balloon is inflated with air.

part of the duodenum. The stylet is then pulled out. (Fig. 4.)

In order to remove the wire more easily, 10 cc. of mineral oil should be injected into the Miller-Abbott tube. By grasping the wire with a hemostat and exerting a steady, forceful pull the stylet is removed. Because of the angle around the pylorus, considerable force has to be exerted. The position of the tip of the tube is again verified and 20 to 25 cc. of air is injected into the balloon. The tube is advanced 6 inches further into the stomach. The patient is kept in the fluoroscopic room until the tube has entered the jejunum. Aspiration of the duodenal contents aids in the progression of the tube down into the jejunum. When the tube's slack in the stomach is seen to be gone, 6 inches more of tube is advanced from above in order to keep it lying along the greater curvature. It is usually only a matter of minutes until the tube passes the ligament of Treitz.

PROGRESS OF INTUBATION

With the patient back in his room intermittent suction is applied and the tube is advanced at the rate of about 6 inches an hour. Roentgen films should be taken periodically to determine the progress of the tube.

A distinct label is placed on the opening leading to the balloon so that no fluid will be injected into it. The suction section of the tube should be flushed with saline solution about every two hours. Bland liquids may be started by mouth after the 2 foot mark on the tube is reached. As the deflation is completed a special low residue diet is begun. These are foods that will not plug the openings in the Miller-Abbott tube, such as lean meat, eggs, broth, gelatin, custard and thin gruel. Fortunately, they are largely of a high protein nature much needed by these patients.

When the x-ray films indicate complete deflation of the small bowel, the air is removed from the bag and suction is discontinued. If gas is passed by rectum and the patient can eat without discomfort, the Miller-Abbott tube can be safely removed. If one is uncertain of the complete relief of the obstruction, thin barium or one of the new iodine solutions such as gastrografin may be introduced through the tube and roentgenograms taken to determine whether obstruction is still present. If it is, the tube is left in place and preparation should be made for surgery.

If withdrawal of the tube is indicated, it should be done gradually so as not to intussuscept the bowel. On rare occasions the tube has been cut off at the nose and allowed to pass out the rectum.

The junior author, while a resident at Swedish Hospital, was taught the technic of intubation. In twenty consecutive cases of intestinal obstruction he was able to effect passage of the tube into the duodenum in an average of twelve minutes. There was, however, one failure in a patient with a J-shaped stomach but the head of the table was not lowered to take full advantage of gravity. This technic is not 100 per cent successful, but has given us a great deal of satisfaction with only occasional failures.

INDICATIONS FOR USE

A long experience with the Miller-Abbott tube has confirmed, in our opinion, the following indications for its use.

Principal Uses. These include: (1) decompression of adynamic ileus secondary to surgery, trauma, peritonitis, cholecystitis, pancreatitis, renal disease, spinal injuries and pneumonia; (2) simple mechanical obstruction with distention.

It is important to make a differential diagnosis between simple mechanical intestinal obstruction and strangulation. The history of continuous pain, an elevated white blood cell count and a tender abdominal mass should alert the physician to the possibility of strangulation. Even in early mechanical obstruction and strangulation, the preoperative passage of a Miller-Abbott tube may be of great aid in

preventing a postoperative ileus. (The most frequent use of the tube is in postoperative ileus.) This type of obstruction is usually due to surgical trauma and may be completely relieved by decompression.

Secondary Uses. The following secondary uses of the Miller-Abbott tube may be found very useful on occasion: (1) preoperatively in strangulation obstruction and mechanical obstruction without distention; (2) preoperatively in colonic resections; (3) large incisional hernias; (4) treatment of acute exacerbation of ulcerative colitis; (5) prevention of recurrent intestinal obstruction; and (6) localization of tumors of the small bowel and partial obstruction.

It is better not to use mercury in the balloon in patients without obstruction because the tip of the tube will more likely remain at the spot desired when the balloon is deflated. Intubation may be of considerable aid in colonic resections because it helps position the small bowel away from the operative field. It will also permit an earlier feeding program without danger of distending the colon and putting pressure on suture lines.

In the management of large incisional hernias its use prevents the common postoperative ileus with distention.

Intubation may be of considerable value in the treatment of selected cases of acute ulcerative colitis. Thus one may give complete rest to the colon while the patient is fed by mouth, and direct medication through the tube may be applied to the colon.

The use of a long intestinal tube in the prevention of recurrent intestinal obstruction due to adhesions has been tried by the senior author on two occasions with excellent results. This has the same effect as the extensive Noble plication operation. Adhesions are formed over the Miller-Abbott tube in such a manner that there are no acute angulations. Under such circumstances the tube should be left in place for four to five days. Introduction of the Miller-Abbott tube at the time of surgery may be done on the operating table, using a vein stripper as a guide through the pylorus and duodenum.

Tumors of the small bowel may be localized by finding blood in the aspirating fluid or noting stoppage of the balloon's progress down the bowel. An injection of a thin barium mixture or iodine solution through the tube may then localize the point of obstruction. In one case, the source of three massive intestinal hemorrhages was located by finding blood in the suction fluid 1 foot beyond the pylorus. This technic enabled us to find a small adenomyoma of the upper jejunum at surgery that would otherwise have been missed.

CONCLUSION

The Miller-Abbott tube is a highly useful tool in the management of intestinal obstruction and in the diagnosis and management of selected intestinal lesions. Attention to details and the combined use of the wire stylet and mercury bag have made the use of the Miller-Abbott tube a much easier and less formidable procedure.

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DISCUSSION

Charles E. MacMahon (Seattle, Wash.): It certainly cannot be said, or even intimated, that Dr. Loe has been premature in presenting his technic for the rapid passage of the Miller-Abbott tube. I have been after him for the past five years

or more to make a presentation of this very simple and most effective method of small bowel intubation. I first saw Dr. Loe utilize this technic in 1940. At first glance it was obvious that he could introduce the Miller-Abbott tube into the small bowel well beyond the ligament of Treitz quickly and without difficulty. I thought this represented just a peculiar talent that he personally possessed and for a long time after returning to practice after the service in 1946, whenever I felt that a Miller-Abbott tube was indicated, I called Dr. Loe for his help and he always responded promptly. Fortunately, he was not out of town or ill on any of these occasions, and as a result I made no personal effort to master the technic. Recently he asked me why I did not learn to do this myself, particularly since he had great success in teaching the method to a succession of interns and residents.

It is most important to follow his directions in every detail, for it is the summation of attention to each detail, as he has outlined them, that makes possible the quick and successful introduction of the tube through the pylorus into the second portion of the duodenum. A resident surgeon who has never seen the method used can, if he will follow these instructions, almost invariably perform the procedure successfully in about twenty minutes. There is little to add to the excellent presentation that Dr. Loe has belatedly made to emphasize one of the many uses for this procedure.

I would like to comment on a series of x-ray films of a thirty-five year old white man with acute progressive ulcerative colitis. The first film showed a classic ladder pattern of small bowel, with evidence of fluid and inflammatory reaction between the loops. At this instant the patient had a silent abdomen, diffusely tender, and had been running a temperature of 105°F. daily for over two weeks. The decision to perform total one-stage colectomy had been made, and the Miller-Abbott tube was to be introduced for the purpose of decompression preoperatively, and to be maintained postoperatively as an aid in the prevention of the all too common postoperative complication in this procedure, a small bowel obstruction.

The second film showed the bag at the second and third portion of the duodenum, approximately fifteen minutes after introduction into the stomach. The tube rapidly advanced. The third film showed the completely decompressed small bowel twenty-four hours after introduction of the Miller-Abbott tube.

The next film showed the position of maintenance of the Miller-Abbott tube in the postoperative period, the tube having been brought out through a gastrostomy wound at the time of surgery in a fashion not dissimilar to that advocated by Smith and Ferris for postoperative gastric decompression. This allows for maintenance of the tube through the entire length of the small bowel in the postoperative period for an indeterminate period of time without the possible complications and discomfort of nasogastric intubation. In effect it also accomplishes, as Dr. Loe has stated, the same result as the Noble plication procedure.

Finally, I would again re-emphasize the necessity of following his specific instructions explicitly if you are to enjoy the rewards of rapid, easy small bowel intubation when it is indicated.

BERNARD P. MULLEN (Seattle, Wash.): Dr. Loe introduced this tube into a patient of mine who had a stomal obstruction following subtotal gastrectomy for a duodenal ulcer. It would be hard to find a more difficult case in which to pass a Miller-Abbott tube. We watched the tube go through the anastomosis under fluoroscopy. Prior to this nothing seemed to be going through. In this terrible complication following gastrectomy we were able to demonstrate that the anastomosis was open. Following this, even with the tube in place, the stomach refused to empty. However, four months and three operations later the stomach began emptying. We did demonstrate the feasibility of passing a Miller-Abbott tube in these cases.

RALPH H. LOE (closing): I was reluctant to present this paper because it actually presents nothing original; it is merely a combination of other methods.

I first learned about the stylet part of the technic from W. Osler Abbott whose father taught bacteriology at the University of Pennsylvania. He was a genius in his own way and developed the Miller-Abbott tube along with Dr. Miller. The tube was originally used in the study of the physiology of the small bowel.

Unfortunately, Dr. Abbott died of leukemia in 1943 so we have lost the advantage of his outstanding ability.

Surgical Treatment of Ulcerative Colitis

A COMPARISON OF SINGLE-STAGE COLOPROCTECTOMY WITH OTHER PROCEDURES

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CHRONIC ulcerative colitis becomes a surgical problem once it has reached the stage when it no longer responds to medical therapy. Irreversible degenerative and ulcerative changes with associated toxic absorption, severe intractable diarrhea, dehydration, malnutrition, repeated severe hemorrhages, perforation, incontinence and obstruction are among the conditions which call for surgical intervention. The possibility of the development of cancer is also to be considered if the disease remains active for a period of years. Hickey and Tidrick [1] found in their study that cancer of the colon developed in 29 per cent of patients known to have had ulcerative colitis for ten years or longer.

Although surgical therapy has gained general acceptance for the treatment of advanced forms of the disease, there is still a difference of opinion as to the merits of the various types of operations which have been devised for its treatment. Controversy centers principally on whether the operation should always be total coloproctectomy or whether lesser procedures such as colectomy with ileoproctostomy are sometimes justified.

In order to assess the merits of the several methods in our own experience, we have reviewed the results in the forty-two patients operated upon in the Veterans Administration Hospital, Long Beach, in the seven-year period from January, 1952 to January, 1959. The operations performed were of three general types: (1) less than total resection of the colon, rectum and anus, (2) total resection and ileostomy in planned multiple stages, and (3) total resection and ileostomy in one stage [2].

The ages of the patients in this study correspond to the ages generally reported for the onset of the disease and the time of operation. The youngest at the time of the onset of symptoms was nineteen years of age, and the oldest fifty-three. The youngest patient at the time of the primary operation was twenty-three years of age, and the oldest sixty-one.

Most of the patients had received prolonged intensive medical therapy prior to surgical treatment. The exceptions were patients operated upon because of uncontrolled hemorrhage or perforation. The interval between the recognized onset of the disease and surgical therapy varied from one month to fifteen years, with a mean interval of six years. The degree of debilitation at the time of operation was usually proportional to the duration of the disease, but there were notable exceptions in which fulminating attacks occurred at the outset. The prior medical therapy consisted of programs in which antibiotics and corticoid drugs played a dominant role. The seventeen patients (40.5 per cent) who received either cortisone or adrenocorticotropic hormone therapy showed varying responses to these agents. Cortisone therapy gave relief for no more than a few weeks. In general there was progressively poorer response with repeated courses. Psychotherapy was used in several of the patients without apparent success, but its use was too infrequent and of too short duration to afford an opportunity to assess its value fairly.

The indication for surgical treatment in all the patients was the presence of disease of the colon which was severely debilitating and could not be controlled by medical means. (Table 1.) Severe intractable diarrhea was present in 79 per cent, recurring bouts of hemorrhage in

TABLE I
INDICATIONS FOR SURGICAL TREATMENT*

Indications	No. of Patients
Diarrhea	33
Bleeding	27
Weight loss	13
Obstruction	3
Abdominal mass	2
Perforation	1
Sepsis	1

* Some patients had several indications.

64.5 per cent, extreme loss of weight and general sepsis in 31 per cent, and obstruction in 7 per cent. An anal fistula with single or multiple tracts was present in seven patients. Three patients had duodenal ulcers with histories indicating that the onset of duodenal ulcer followed the onset of the disease of the colon. Less frequent complications and sequelae were perforation, malignant degeneration and arthritis.

Roentgenographic examination and sigmoidoscopy were the principal objective means of demonstrating the gross pathologic changes. The roentgenographic examination was accurate in establishing the presence of the disease, but it failed to show the extent in half the cases. It was not infallible in determining the presence of polypoid changes. The changes commonly seen with sigmoidoscopy were ulcerations, congestion, edema and polypoid changes. Bleeding with contact of the instrument against the mucosa was a usual occurrence.

All the excised specimens of colon showed large areas of ulceration with various degrees of fibrosis, thickening, congestion and edema. Ninety-three per cent of the specimens showed mucosal polypoid changes. The rectum showed edema, congestion, ulceration and fibrosis in all the cases of total coloproctectomy and was more seriously affected by the disease than other portions of the excised tract.

Cancer was demonstrated by microscopic examination in five of the specimens (12 per cent). The cancerous changes were confined to the cecum and ascending colon in two cases, to the sigmoid area in one case and to the rectum in two cases. Four of the five cases of cancer were in young patients between the ages of twenty-seven and thirty-five years.

TABLE II
PRIMARY SURGICAL PROCEDURES

Procedures	No. of Patients
Group 1: Less radical than total colectomy:	
Subtotal colectomy with ileostomy or colostomy	18
Colectomy with ileoproctostomy	4
Anterior resection	2
Colostomy	2
Group 2: Planned multiple-stage total colectomy	4
Group 3: One-stage total colectomy	12

SURGICAL TREATMENT

Group 1. Twenty-six patients had initial procedures less radical than total coloproctectomy. The procedures used in these operations were simple ileostomy, ileoproctostomy, ileostomy and partial colectomy with establishment of a sigmoid fistula, colectomy and ileoproctostomy, and hemicolectomy with or without colostomy. (Table II.)

Eighteen of the twenty-six patients had additional surgical procedures because of unsatisfactory results with the primary operations. One patient died of cancer of the colon one month after a secondary operation. The primary operation in this case, anterior resection of the sigmoid colon, had been performed two years earlier. It is probable that this cancer death would have been averted if total coloproctectomy had been performed initially. One patient, a young woman, had a massive hemorrhage one year following simple ileostomy. She failed to survive emergency resection of the colon performed to arrest the hemorrhage. The other sixteen were well after the secondary procedures.

Of the eight patients who did not have secondary operations, three died of the disease. One of the deaths was due to perforation of the large bowel with generalized peritonitis. Another death occurred as the result of cancer which became evident one and a half years after right hemicolectomy. The third death was from pulmonary embolism which occurred three days after subtotal resection of the colon with establishment of an ileostomy and a sigmoid fistula. This patient, a severe diabetic, was in

extremely poor condition at the time of operation and the outcome was probably not influenced by the limited type of procedure.

The five surviving patients in the group with operations less radical than total colectomy and without secondary procedures have not fared well postoperatively. All were having severe difficulties when last seen after two or more years of follow-up. The principal disturbances were severe diarrhea, malnutrition, bleeding and anal fistula formation. All were advised to have secondary operations for removal of the remaining diseased bowel but they refused or were lost to follow-up.

Group 2. Four patients underwent planned two-stage total coloproctectomy with ileostomy. The eventual results were satisfactory in all the patients, although disability was prolonged for several months in each case because of the division of the operation into stages.

Group 3. Twelve patients underwent one-stage total coloproctectomy and ileostomy. There was one surgical death which occurred three days after an emergency operation for massive bleeding. The immediate cause of death was coronary vessel disease. With the exception of this case, the results were uniformly satisfactory. There was early restoration of health and return to the former status of activity. All recovered from the severe state of malnutrition and debilitation from which they had previously suffered. The only significant postsurgical complications were several ileostomy disturbances in the early cases which required revision.

The type of ileostomy has had an important bearing on the postoperative course. A protruding type of ileostomy was made in the early cases. (Table III.) This resulted in complications of prolapse, stricture and fistulas which made surgical revision of the ileostomies necessary. In the past several years we have used the flush type of ileostomy [3]. There have been few complications and most have required no more than minor procedures for their correction.

TABLE III
ILEOSTOMY COMPLICATIONS

Complications	Type of Ileostomy*	
	Flush	Protruding
Revisions	4	7
Prolapse	3	2
Stricture	1	3
Fistula	0	2

* Twenty-five flush-type and nine protruding-type ileostomies were carried out.

CASE REPORTS

Representative cases have been selected from each of the three groups to illustrate the preoperative condition of the patients, the operative course and the results of the several methods employed.

Group 1: Planned Operations Less Radical than Total Coloproctectomy

J. L., a thirty-two year old milk salesman, was admitted on July 10, 1957, with the complaint of diarrhea and bleeding. The diagnosis of chronic ulcerative colitis had been established five years previously, and the patient had been treated with various programs of medication including steroids, Banthine,® Sulfathalidine® and special diets during the two years prior to admission. X-ray examination showed typical changes of ulcerative colitis in the descending and sigmoid colon. Sigmoidoscopic examination showed ulceration of the mucosa. Total colectomy was advised but was not accepted. Therefore, a less extensive operation consisting of ileostomy and partial colectomy with establishment of a sigmoid fistula was performed on September 30. The rectum and distal part of the sigmoid were not removed. The patient continued to have bloody purulent discharge from the rectum and there was no improvement in his general condition. He returned to the hospital seven months later because of severe rectal bleeding. Proctoscopic examination showed persistence of the ulcerations and pseudopolyposis with multiple sites of bleeding. Emergency operation consisting of removal of the remaining portion of the large bowel was performed on April 30, 1958, to arrest the bleeding. There was immediate relief following the second operation with gain in weight, and the patient returned to his former employment one month later.

Group 2: Planned Multiple-Stage Total Coloproctectomy with Ileostomy

H. G., a twenty-eight year old newspaper manager, was admitted on April 7, 1953, with exacerbation of symptoms of chronic ulcerative colitis. The disease had been present for years. Treatment with special diets, antibiotics, corticotropin and cortisone was associated with short periods of remission. At the time of the current

admission he was suffering from severe diarrhea, bleeding and fever. There had been a 35 pound weight loss in the previous six months. X-ray examination showed a short tubular colon. Proctoscopic examination disclosed an ulcerated, friable, bleeding mucosa with pseudopolyposis. The patient was cachectic and anemic. Subtotal colectomy and ileostomy was performed on May 4 as the first stage of a planned two-stage total coloproctectomy. The manifestations of the disease remained unchanged following the first-stage procedure. The total resection was completed on October 20, four and a half months after the first stage. Following this the patient rapidly regained his health and he returned to his former occupation in four weeks.

Group 3: One-Stage Total Coloproctectomy with Ileostomy

J. J., a twenty-six year old restaurant cook, was admitted on November 17, 1958, with abdominal pain, weakness, diarrhea and recurrent fistula in ano. His disease had existed for six years. Treatment with special diets, antibiotics and cortisone had failed to arrest the progress of the disease. The patient was having ten to twelve bloody bowel movements daily at the time of admission. X-ray studies showed a shortening of the colon and pseudopolyposis. Proctoscopic examination to 25 cm. showed a friable, ulcerated mucosa which bled easily with contact of the instrument. The hemoglobin was 12 gr. per cent. Single-stage total coloproctectomy with ileostomy was performed on December 11. The specimen showed inflammatory changes of the terminal 15 cm. of the ileum, and ulcerations and pseudopolyposis of the colon. The patient made a good postoperative recovery with a weight gain of 10 pounds in the first six weeks. He returned to his former occupation five weeks after the operation.

Group 3: Emergency One-Stage Total Coloproctectomy with Ileostomy

H. M., a twenty-three year old laborer, was admitted on May 30, 1956, with a history of fever, diarrhea, bloody mucous stools and a loss of weight of approximately 100 pounds over a period of a year. Blood transfusions were given a week before admission and on the day of admission because of severe loss of blood. The hemoglobin readings remained low following the transfusions. Proctoscopic examination disclosed ulcerations, edema and congestion of the rectum. Total coloproctectomy with ileostomy was performed on May 31 as an emergency procedure. There was rapid restoration of health and a gain in weight of 40 pounds in the weeks following the operation. He returned to work several weeks later.

COMMENTS

Our results lead us to the opinion that when surgical therapy is required for the treatment of ulcerative colitis the procedure should be total coloproctectomy with ileostomy. All the cases of total resection in this series have had successful outcomes except the one surgical death in an emergency operation for hemorrhage, while the results of lesser procedures including ileostomy, partial resection of the colon with end-to-end anastomosis of the ileum to the rectum, and partial colectomy with ileostomy or colostomy have been poor without exception. We had hoped that resection with ileoproctostomy would control the disease but this hope has not been realized. The four patients who underwent this procedure required later excision of the remaining anorectal segment because of post-surgical occurrences of anal fistulas, bleeding, purulent discharge and incontinence. The failure of the anastomotic procedure is not surprising in view of the fact that the rectal segment is more vulnerable to the disease than any other part of the large bowel. Other procedures less radical than total excision were equally unsatisfactory. Two deaths occurred in patients with partial colectomy, one from hemorrhage and the other from cancer. These deaths would probably have been averted if all the diseased tract had been resected at the initial operation. Most of the other patients with procedures less radical than total resection had subsequent conversions to total coloproctectomy. Others refused further resection or were lost to follow-up.

Our experience convinces us that total coloproctectomy with ileostomy should be done in one stage rather than in multiple stages. The advantage of the one-stage procedure is that it is accomplished with less postoperative morbidity and an earlier return of the patient to normal activities. This is probably explained by the fact that the source of the toxic absorption is removed at once. The one-stage operation has been well tolerated except in the one instance of emergency operation for massive bleeding cited previously. The surgeon need not be committed to completion of the operation in one stage. If the patient's condition is such that the operation should be discontinued, this can be done at any stage and the operation can be completed later.

The permanent ileostomy feature of total

coloproctectomy has been well accepted by the patients. (Table III.) After years of suffering and invalidism from the unremitting disease, they look upon ileostomy as a small price to pay for the relief which they obtain from their distressing symptoms of general toxicity, discharge of bloody purulent material, anal fistulas and perianal skin excoriation.

It is our opinion that sterility, which occurs commonly following adequate abdominoperineal resections for carcinoma, is not as likely to occur in resections for removal of the rectum in chronic ulcerative colitis. In the latter, the dissection is made close to the rectal wall and is not likely to disturb the nerve elements of the sacral plexus.

SUMMARY

We would sum up our attitude as favoring total coloproctectomy when ulcerative colitis becomes intolerable and is no longer responsive to medical management. Medical management should be continued as long as the patient is able to adjust himself to the disease.

We favor one stage over planned multiple stages for total resection with ileostomy because it brings immediate relief to the patient without a prolonged convalescence in which complications may arise and in which the patient suffers economic loss. Surgical mortality does not appear to be a factor against the one-stage procedure. The immediate postoperative convalescence is more satisfactory than with multiple-stage procedures probably because of the immediate and total removal of the source of the toxic absorption. While multiple stages may give the patient an opportunity to adjust to the acceptance of permanent ileostomy during the weeks or months between stages, we do not believe this is an important enough consideration to weigh against the use of the one-stage procedure.

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DISCUSSION

William P. Mikkelsen (Los Angeles, Calif.): Drs. McLenathen and Weinberg have made an important contribution to the growing amount of evidence supporting the contention that any procedure short of total coloproctectomy with ileostomy for chronic ulcerative colitis is insufficient. Furthermore, they present convincing evidence to justify their opinion that in the majority of cases the operation should be conducted in a one-stage maneuver. Even in the severely debilitated patient, total resection of the colon is frequently well tolerated. In certain of these instances it is perhaps unwise to terminate the operation short of this. Nevertheless, good judgment would dictate in certain instances that proctectomy be deferred to a second operation. This phase of the total operation, I believe, is the more traumatic, time-consuming and sanguineous, and occasionally is better deferred. In contrast, extreme operative conservatism, as exemplified by simple ileostomy, is probably never justified in the light of current knowledge. The addition to ileostomy of subtotal colectomy with establishment of a sigmoid mucous fistula can be carried out with alacrity and is minimally traumatic. Furthermore, this exhumes the major portion of a fetid, diseased structure that contributes to general toxicity.

The recommendation is frequently made that proctectomy be deferred in a young man because of fear that sexual impotence or sterility may occur. This premise is probably no longer tenable according to information to the contrary supplied by Stahlgren and Ferguson.

Finally, although not emphasized by the authors, it is germaine to consider briefly the association of colonic and rectal carcinoma in chronic ulcerative colitis. Fear of development of this important complication is one of the indications for surgery in this disease. Perhaps this is not a justified indication if it is true, as has been commonly quoted, that in but 5 per cent or so of such cases carcinoma develops. On the other hand, the almost uniform failure to cure such patients lends this figure more significance. Of major importance, thus, is the necessity for data that would permit a more accurate selection of those patients in whom carcinoma is likely to develop. In this connection, of the important features, two deserve a greater degree of recognition than has formerly been given. The first is the duration of the disease process. Although rather wide discrepancy exists in reported series, it is likely that an incidence of carcinoma of greater than 10 per cent after ten years and greater than 20 per cent after twenty years of disease are conservative estimates. Furthermore, quiescence of chronic ulcerative colitis does not guarantee freedom from carcinoma. The second important

feature to be considered is the age of the patient at the onset of the disease. The onset of chronic ulcerative colitis in a patient under the age of twenty renders this patient 500 times more likely to develop colonic carcinoma than a non-diseased person of similar age. This figure is in contrast to the patient who contracts the disease after the age of forty-five; he is but five times more vulnerable to carcinoma than a non-diseased person. Thus, application of these facts would seem to make it almost imperative that colectomy be recommended in a patient thirty-five years of age who has had symptoms of chronic ulcerative colitis for twenty years, and increasingly strong consideration for colectomy should be given to those patients with less imperative surgical indications.

ERIC R. SANDERSON (Seattle, Wash.): I think it should be pointed out that ulcerative colitis is not always a generalized disease. We do occasionally see patients who have localized ulcerative colitis and on whom it is not necessary to perform surgery as extensive as total colectomy.

I would like to present three cases in support of this thought. The first patient, a woman in her late thirties, had a history dating back to 1937. At that time she started to have diarrhea and bloody stools recurrently to the point where she was debilitated and socially embarrassed. Repeated x-ray films showed only a 6 inch segment of sigmoid colon, interpreted as ulcerative colitis. Therefore, in March, 1954 segmental resection of a small piece of the sigmoid was performed.

After excision the patient was in reasonably good condition for six months and she was quite happy. At the end of six months, because of inadequate resection, she began to have recurrence of her symptoms. I observed her for a year after her primary surgery, and then feeling what had been done was correct in theory but incorrect in practice, I performed resection a second time.

At the time of the second operation excision was performed from the middle of the transverse colon to the upper portion of the rectum, and end-to-end anastomosis was carried out at that point. The pathologist assured me repeatedly that this was typical ulcerative colitis.

Since March, 1955 (the time of re-resection) she has been without symptoms.

The next patient, a sixty-five-year old man from the tropics, had had a seven-year history of recurrent diarrhea with bleeding. He had been assured by his physician that everyone in the tropics had this sort of thing and it was to be expected. However, barium enema examinations showed a 6 inch segment of sigmoid with one polyp and what was thought to be a poorly prepared bowel above it. Therefore, sigmoidoscopy was performed with the thought that the polyp could be removed. It was apparent at the time of sigmoidoscopy that he had many pseudopolyps typical of advanced ulcerative colitis.

At laparotomy he was found to have a segment of 100 or more tiny pseudopolyps. This is typical of chronic ulcerative colitis.

He was operated upon only recently so although he is asymptomatic at the present time I cannot give you a long term evaluation.

An incidental finding of interest in this case was an aneurysm of the splenic artery, which was excised one month after operation for colitis.

The final patient, a woman in her sixties, had had her appendix removed about three years previously. For the preceding six months to the time I saw her she had had right-sided abdominal pain. After study, we concluded that the right colon was the site of disease, which we interpreted as carcinoma. In October, 1955, surgery was performed.

Ulcerative colitis involved the terminal ileum and the right colon. Right colectomy was performed with end-to-end ileotransverse colostomy. No symptoms referable to recurrent ulcerative colitis have developed so far.

I think one aspect of ulcerative colitis is localized segmental ulcerative colitis for which limited resection is adequate treatment. I do not think this is discussed as frequently as it might be and that is why I brought it up now. I am sure that there must be many other patients similar to the three I have presented.

CLARENCE J. BERNE (Los Angeles, Calif.): I would like to change the subject from the surgical management of chronic ulcerative colitis to the problem of the ileostomy.

In Los Angeles we have had some experience with a rather active ileostomy club. There are two publications available to surgeons and their patients: "The Ileostomy Quarterly" and a newsletter of the Ileostomy Association of Great Britain. One can get both of these sent to his office regularly; they have much valuable information for the surgeon and many aids for the patient. I think this is worthy of emphasis because after successful recovery from colectomy these patients have their ileostomies for the rest of their lives, and after a few years this total experience actually is judged in terms of their satisfaction with the ileostomy.

I would like to refer to a point in the paper of Drs. McLenathen and Weinberg, that of a flush ileostomy. This operation has been presented before by Dr. Weinberg's group.

I am of the opinion that a flush ileostomy is less satisfactory than a protruding ileostomy. Much can be said about technics for this, and all of them are the same in principle if the ileostomy has some length, an outside epithelial (mucosal) cover and no granulation tissue. It does not matter much with which one of the standard technics this is obtained. I prefer the Allan Brooke.

An ileostomy about 1 to 1½ inches in length is better than one that is too long. If one investigates these matters with a number of patients in an ileostomy club, the first basic principle the patients want is to have the ileostomy as near the midline as possible. The surgeon, of course, wants it as far lateral as possible because the gutter closure problem is thereby minimized on the inside.

Many patients find that their ileostomies are either too high or too low. There is a problem in deciding where they should be. However, if one studies his own body, while seated upright in a straight back chair, and bends forward sharply, he will find that his abdomen develops a primary and secondary flexion crease. A major flexion crease usually exists at the line of the umbilicus so that the plate must have room between the stoma and the primary flexion crease. If the stoma is too high, the plate will lie over the flexion crease and also constantly annoy the patient at his belt or her waistline. More important, it will be drawn into problems with the primary flexion crease. If it is too low the disc will strike the thigh. Therefore, the vertical and transverse positions in the frontal plane are both of great importance to the patient.

I think that the surgeon should study the problem by sitting erect and putting the ulnar side of his own right hand against his lower abdomen, sliding it downward against his groin with his thigh flexed at right angles, and then putting his thumb at his primary flexion crease. When he bends over sharply he will ascertain that he has outlined an area of abdomen, the center of which is the best site for the ileostomy.

I know most of these points are controversial but I will summarize by saying that the ileostomy itself is tremendously important to the patient. The patients with whom I have had contact through the club are much happier if they have an ileostomy with length rather than a flush ileostomy, and it is very important to them how high or low it is and where it is in relation to the midline.

ALLEN M. BOYDEN (Portland, Ore.): Our treatment of total ulcerative colitis, eliminating such fortunate patients as Dr. Sanderson mentioned, has changed markedly. I am sure the surgical answer to this disease today is infinitely better than it was in 1945, for example.

We have learned that most of these patients can be operated upon in one stage consisting of total colectomy and an adequate ileostomy which will function almost immediately. For about five years we have performed only one-stage colectomies upon patients who have total involvement of their colon.

I have been using the flush type of ileostomy ever since Dr. Weinberg's group reported on it to this Association several years ago. I have found myself revising the old type of ileostomy in patients who have trouble to a flush-type ileostomy, and most of these patients are better satisfied. I find that most of the flush-type ileostomies do not remain flush with the skin but have a small protrusion. They will accept the bag without leak and without difficulty equally as well as the protruding type of ileostomy.

In the last several years I have developed what I believe to be a minor improvement in the technic of making such an ileostomy. I have been disturbed by the small fistulas or stitch sinuses that occur when one sutures the skin to the mucosa of the small bowel. These sutures also produce a distortion of the circular aspect of the ileostomy.

I prepare this ileostomy in the same manner as a subcuticular suture of a superficial wound or an abdominal operative wound. By using very fine catgut on "swedged" needles and taking a subcuticular stitch through the sero-muscular layer at the cut edge of the ileostomy and the subcuticular layer of the skin, and dividing the bowel into segments (quarters, eighths and then sixteenths), one can produce a sealed wound almost immediately. In one case, the suture line was completely healed on the seventh day. There was no evidence of granulation and no sinus where the sutures were placed. This procedure takes a little more time but has been very rewarding to me.

CHARLES E. MACMAHON (Seattle, Wash.): I would like to support Drs. Weinberg and McLenathen's approach to this particular problem in one specific group of cases within the large group of patients with ulcerative colitis, emphasizing a point that Dr. Mikkelsen made in his discussion.

The patients who die of this disease usually fall into the category of those with acute florid fulminating progressive ulcerative colitis with peritonitis. These are the patients who are critically ill with temperatures of 104 and 105°F., and who have usually worn out three or four internists while they are making up their minds whether intervention is indicated. I think the procedure can more safely be performed in one stage than in two or more stages. This was well pointed out by Dr. Scarborough before this Association a few years ago. His mortality rate was, as I recall, not much greater than 1 per cent in a rather large series.

The point that Dr. Mikkelsen made was that the most traumatic part of the procedure is the posterior dissection, which ordinarily comes at the end of this operation.

I have used a minor variation in five cases of acute progressive ulcerative colitis and reported it to the North Pacific Surgical Society last November. It merely amounts to doing the procedure wrong end-to. This consists of placing the patient in the Buie position and performing the posterior dissection initially. Approximately fifteen to twenty minutes are needed to mobilize the rectum below the pelvic floor. Then, reversing the patient

into the supine position, you progress from left to right. The total length of operating time in my experience has never been in excess of three hours. I think the patient, separated from this acute inflammatory process that is about to kill him, is in a safer situation than with a staged procedure.

My experience with these five patients has been most gratifying, without mortality and with minimal morbidity.

ROBERT A. SCARBOROUGH (San Francisco, Calif.): I think it is quite obvious from this extensive discussion that surgeons have developed much more enthusiasm for surgery in chronic ulcerative colitis than they had ten years ago. When Dr. Emmett Allen was an invited guest in San Francisco at a general meeting of the county society, he gave as the only indication for surgery in ulcerative colitis the internist and the patient coming to the surgeon and begging for operation. We have certainly advanced a long way since then.

I would like to comment on a few points in this paper. First, the primary definitive operation for this disease is colectomy, although people still speak of ileostomy as the primary procedure. We all realize now that that is the secondary but necessary procedure, unfortunately, in dealing with the disease surgically.

We are also coming to learn that we have a lower operative mortality, fewer postoperative complications and a well patient in a much shorter period of time if we perform the entire procedure as a single-stage operation.

Ileostomy alone leaves behind the diseased bowel with its toxic manifestations, its impending or prior or subsequent complications, and we must remove the diseased bowel.

At the present time, of course, there is considerable enthusiasm, initiated, I think, principally by Mr. Aylett of London, to perform resection and save the rectum and anastomose, at the same time or at a later date, the ileum to the rectum. This idea is sweeping the country in certain areas with an enthusiasm I feel is going to end in great disappointment.

Three patients have been mentioned in whom the rectum could be saved and resection performed with re-anastomosis. There are occasional cases which encourage us to perform a re-anastomosis in chronic colitis.

We have actually had twelve such patients but we do not consider them as patients who had chronic idiopathic ulcerative colitis. They have had segmental colitis, and certainly in those cases in which the rectum is not involved at all such resection and anastomosis can be performed. However, in the typical disease the rectum is the most severely and usually the first portion of the colon to be involved, and that portion of the colon must be sacrificed.

The four cases of ileoproctostomy mentioned in this paper all resulted in failure, and ultimate resection of the rectum was necessary. That has been our experience in the past. We have resumed attempts to do the same thing again because of Mr. Aylett's experience and that of a few others. To date, no patient upon whom we have performed anastomosis of the ileum to the rectum has been able to retain his rectum. All have had to have subsequent resection and ileostomy.

Regarding the type of ileostomy performed, we have spoken of the flush type and the protruding type. I think the important thing here is the improvement we have in the technic of performing primary anastomosis of the end of the ileum to the skin which prevents chronic inflammatory changes with stricture and mechanical obstructive features. The important thing is not the type of ileostomy performed; it is important that primary anastomosis of the open end of the ileum to the skin is effected so there will be no necessity for maturation of the ileostomy. It will heal per primam.

Actually we can combine the ideal primary anastomosis of the end of the ileum to the skin with some protrusion. The real point of this procedure is that in the formation of the ileostomy, the mesentery of the bowel within the abdomen be attached to the anterior abdominal wall in such a manner that there will be a redundancy of ileum passing through the abdominal wall to the outside. With that as a fixed point you can turn back the open end of the ileum. You are not conscious that you are turning it back but it does evert. You suture the skin and then normal peristaltic activity produces a certain protrusion which is better mechanically in the subsequent care of an ileostomy.

I would like to make one point about the problem of sterility. There is no reason for sterility after resection of the rectum for ulcerative colitis. The important thing is to stay close to the bowel when you resect the rectum as you go down through the pelvis. If you do, this problem will not arise.

Finally, as far as the possibility of cancer as an indication for surgery, I agree with the former discusser that when the disease has been present for a long time this is a real threat; if it should occur before colectomy, the chances for cure are small.

LESTER R. CHAUNCEY (Portland, Ore.): I hate to prolong this discussion much longer, particularly because my remarks must necessarily be based upon a relatively small series of cases. However, I would like to say something in support of the attempts made to save the rectum in the treatment of this disease. Usually these attempts fail. Drs. McLenathen and Weinberg recorded four such procedures, all of which failed. In his discussion Dr. Scarborough mentioned twelve more instances and all of these failed also.

However, not all attempts fail. About six years ago we performed two such procedures. Both patients were young women in their thirties with fulminating disease, one of whom had suffered a perforation of the cecum. In each instance, after the establishment of an ileostomy, subtotal colectomy was performed but the rectum was saved and brought out as a low-lying colostomy. After a two-year interval the ileostomy was taken down and ileoproctostomy performed. In one of these instances the attempt failed; because of recurrent massive hemorrhage the lower bowel was subsequently removed and a permanent ileostomy established. However, the second case was not a failure. This young woman is quite well five years later. Her marriage had been threatened by divorce, the husband being unable to tolerate the ileostomy. Now, five years later, the wife is an active high school teacher and her marriage has been saved. The daily need of tincture of opium plus the occasional removal of edematous polyps from the rectum seem to be a small price to pay for her well-being.

Furthermore, I think we must realize that in spite of what types of ileostomies we might establish, flush or otherwise; in spite of what journals the patient may read; in spite of what help he may receive from ileostomy clubs; the basic fact still remains that no one really likes an ileostomy. This is particularly true of younger children. In the present state of our knowledge of this disease, I think it is wrong to commit a young boy of fourteen or fifteen irrevocably to life with a permanent ileostomy when the lower segment could be saved without detriment to his health.

Gordon Smith (Los Angeles, Calif.): I would like to make two points in regard to the critically ill patient who is a candidate for surgery for ulcerative colitis. One is the use of mild hypothermia in the very septic patient. On several occasions we have used this and found that the patient will tolerate the one-stage complete operation very well.

The second is the use of the two-team procedure for the operation. It decreases operating time almost 50 per cent. We believe it facilitates the perineal part of the dissection, and I recommend this to your attention.

Leon Goldman (San Francisco. Calif.): I think there are two reasons for the improvement in results following the present day treatment of ulcerative colitis. First, the results of surgical treatment have proved to our medical colleagues that we can operate upon these patients with a reasonable mortality rate and a high index of cure; hence patients are referred earlier. It was not very long ago that we could not offer such hope. The second factor is in good part due to the contributions of Ripstein of New York who showed that, paradoxically, it was more important to remove the colon in the treatment of acute ulcerative colitis than it was in the treatment of the chronic disease. As Dr. Scarborough just mentioned, the patient is apt to have a rather hectic postoperative course if the colon remains and thereby continues as a toxic focus.

Another point I would like to make is that any operation for ulcerative colitis in which the diseased bowel is anastomosed involves considerable danger from such complications as a leaking stoma, abscess, peritonitis or even death. As the authors have shown, patients undergoing the lesser procedures have a higher immediate mortality rate, lower cure rate and higher index of recurrence.

Caleb S. Stone, Jr. (Seattle, Wash.): I would like to support the authors' contention that the one-stage procedure serves a very important purpose.

Some four or five years ago Lucius Hill and I presented the technic of total colectomy and proctectomy accomplished from above. We had a fairly small series of cases at that time. We have used this operation consistently in the treatment of ulcerative colitis and it has proved extraordinarily satisfactory. It saves about thirty minutes or more in operating time, and avoids the necessity of turning the patient (usually in critical condition) at the end of a long operation. We have encountered no difficulty in the accomplishment of colectomy and proctectomy in this one-stage procedure, all done from above, and I can recommend it to you very highly.

Joseph A. Weinberg (closing): Dr. McLenathen and I are pleased with the response to our presentation. We realize that this is due to the importance of the subject to everyone and that it is somewhat of a controversial subject. The comments of the discussers lead us to believe that there is less difference of opinion now than there was a few years ago.

We are in agreement with Dr. Mikkelsen that there may be patients who appear poorly suited to withstand one-stage total resection. However, the more experience we have, the fewer occasions we find for multiple stages.

In regard to Dr. Sanderson's remarks, I do not think we have serious disagreement, even though Dr. Sanderson might be understood as favoring less extensive resection. I do not consider his third case one of chronic ulcerative colitis. I interpret it as a combination of regional ileitis and colitis, a disease which calls for less extensive resection. I know that Dr. Sanderson must have his good reasons for classifying it as chronic ulcerative colitis and I may be in error in my interpretation.

Regarding Dr. Berne's remarks about the type of ileostomy, our patients with the so-called flush type of ileostomy have been so well satisfied with the operation and our complications have been so

minimal that we feel obliged to continue advocating this type.

With regard to Dr. Boyden's comments, we appear to be in complete agreement. We are pleased to have some new angles on the performance of the ileostomy. We certainly shall look into it further as a way of improving the operation.

Dr. MacMahon's procedure of reversing the order of excision seems to be an excellent idea. His reasons for performing the anorectal dissection first and then turning the patient for completion of the resection appear to make good sense.

As to Dr. Scarborough's remark that we have advanced from the time when the indications for surgery were strong pleas on the part of the patient and his physician that something be done surgically, we agree that one should not wait for exsanguination, fistula formation and other such serious complications before advising operation, but we still like to have the patient insist that the operation be performed before we take the step of giving him a permanent ileostomy.

About Dr. Chauncey's remark on anastomosing the ileum to the rectum, we had hoped earlier that this could be satisfactorily accomplished. We were encouraged in this thinking by Aylett's reports of successes. However, our experience was poor without exception when this procedure was resorted to and this, together with the experience cited by others, has caused us to abandon the operation of ileoproctostomy except in special instances. For example, we would give the ileoproctostomy a trial in the case of a young person, having in mind that conversion to complete coloproctectomy with permanent ileostomy might be necessary at some time in the future.

We should give consideration to Dr. Smith's remark about two teams working simultaneously, especially when teams can be easily arranged for. Time is an important factor in these seriously ill patients, and it is certainly worth giving a lot of thought to.

We are happy to hear Dr. Goldman emphasize the special need for total coloproctectomy in acute fulminating exacerbation of the disease when seemingly one would want to do the least possible because of the patient's poor condition. We agree with Dr. Goldman that one must do the most rather than the least if anything is to be accomplished.

We wish to thank Dr. Stone for his valuable suggestions for improving the technic of the operation.

Volvulus of the Cecum or Right Colon

A STUDY OF FOURTEEN CASES

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VOLVULUS of the cecum or right colon causes an unusual type of acute intestinal obstruction which is deceptive in diagnosis and often has a fatal outcome. Since this condition was first described by Rokitansky in 1841 [7] numerous reviews and case reports have appeared in the medical literature [1–5,8]. Volvulus of the cecum or right colon is a relatively common cause of intestinal obstruction in certain portions of Eastern Europe, Turkey and India, but it accounts for only about 1 per cent of the cases of intestinal obstruction in America and Britain [7]. The basic etiologic problem in this condition which permits the volvulus or twisting to occur is inadequate fixation with hypermobility of the ascending colon. Delay or confusion in diagnosis may result in death. In a large collective review by Donhauser and Atwell [3], the operative mortality was stated to be 39 per cent. This is a study of fourteen cases of volvulus of the cecum or right colon, with special emphasis on certain clinical features, methods of early diagnosis and treatment.

CLINICAL FEATURES

Volvulus is a torsion or twisting of the bowel and its mesentery producing luminal obstruction and occlusion of the mesenteric vessels. The occurrence of a volvulus involving the right half of the colon or cecum depends on inadequate fixation of these structures. This defect in fixation most often involves the entire right half of the colon, but it may involve the cecum or the cecum with the ascending colon. Torsion most often occurs in a clockwise direction, but counterclockwise torsion is sometimes present. The severity of the clinical picture is dependent upon the rapidity and the tightness of the twisting process, rather than upon the number of complete turns. This tightness and rapidity of the twist are directly related to the early appearance of gangrenous bowel changes. Certain factors such as previous abdominal operations, pregnancy, mesenteric lymphadenitis, tumors, dietary extremes and foreign bodies may predispose to volvulus in a patient who has hypermobility of the right colon. Such a volvulus may also appear as a postoperative complication of abdominal operations, and it is particularly confusing under these circumstances.

A study of the clinical features of this group of fourteen cases of volvulus of the cecum or right colon suggested a clinical classification into two major types. (Table 1.) First, the

TABLE 1
CLINICAL FEATURES OF TWO TYPES OF VOLVULUS OF CECUM OR RIGHT COLON

Acute Fulminating	Acute Obstructive
Rapid, tight, mesenteric twist	Slower twist, more luminal than mesenteric
Gangrene early, common	Gangrene later, less often
Sudden onset, rapid course	Slower onset, longer course
Severe abdominal pain	Pain less prominent
Marked peritoneal irritation	Peritoneal signs less prominent
Simulates abdominal catastrophe	Simulates simple, low, small bowel obstruction
Higher mortality	Lower mortality
Often requires right hemicolectomy	Detorsion, cecostomy usually adequate

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FIG. 1. Case 1. The roentgenogram on the left shows the severely distended cecum located in the pelvis. The roentgenogram on the right demonstrates the depression of the urinary bladder by the distended cecum.

acute fulminating type is characterized by a sudden onset of symptoms, rapid clinical course, severe abdominal pain and signs of peritoneal irritation. Sudden, tight twisting of the mesentery is the basis for these severe, fulminating findings which frequently result in early gangrene of the bowel. This clinical type often simulates other catastrophic abdominal conditions such as perforated peptic ulcer, hemorrhagic pancreatitis or perforated appendicitis. The acute fulminating type is illustrated by the following case report.

CASE 1. E. S., a twenty-five year old Negro man, was admitted to the Los Angeles County General Hospital in July, 1958, because of severe lower abdominal pain associated with dysuria for one day. He was admitted to the genitourinary service because of his urinary complaints. There was no vomiting or generalized abdominal pain. The patient had no previous digestive or abdominal complaints, but there was a history of recent treatment for rheumatic aortic valvular heart disease with subacute bacterial endocarditis.

Physical examination revealed a well developed, well nourished Negro male, complaining of severe lower abdominal pain. He was restless and apprehensive, with a rapid, bounding pulse and a blood pressure of 200/90 mm. Hg. The temperature was normal and the lungs were clear, but the heart was noted to be grossly enlarged with a loud to and fro aortic murmur. There was a large, tender, tense, globular abdominal mass in the suprapubic region. The remainder of the abdominal examination was essentially negative, except for hypoactive bowel sounds. Catheterization yielded a small amount of concentrated urine without reduction in the size of the mass or any relief of the patient's symptoms.

The hemoglobin was 9 gm. per cent and the white blood count was 20,000 per cu. mm. with an increase in the polymorphonuclear cells. The urinalysis was essentially negative.

Scout roentgenograms of the abdomen showed a large gas-filled loop in the pelvis with minimal small bowel distention. (Fig. 1.) A cystogram showed that the dome of the bladder was depressed by the air-filled loop in the pelvis. There was no gas shadow in the right lower quadrant of the abdomen.

Immediate operation was performed with a diagnosis of strangulated volvulus of the cecum. At surgery the volvulus was found to include the cecum and the lower ascending colon, both of which were gangrenous and located in the pelvis. There was a tight clockwise twist of the bowel and its mesentery. Right hemicolectomy was performed and the patient recovered following a difficult postoperative course.

The second clinical variety of volvulus of the cecum or right colon is the *acute obstructive type*. Its chief feature is low, small intestinal obstruction, with intermittent cramping abdominal pain associated with peristaltic rushes, obstipation and vomiting. There are usually no significant physical findings to suggest peritoneal irritation, and scout films of the abdomen usually show a distended small bowel. The clinical diagnosis frequently is low small bowel obstruction. Systemic signs such as fever, leukocytosis and the presence of shock are

usually absent. When gangrene appears in the acute obstructive type, it tends to develop later in the course of the disease. It is usually due to tension ischemic necrosis from high intraluminal pressure rather than from a tight mesenteric twist with mesenteric vessel occlusion. This acute obstructive type of volvulus of the right colon is illustrated by the following case report.

Case 11. F. H., a sixty-nine year old senile Caucasian woman, was admitted to the Los Angeles County General Hospital in June, 1956, because of pain, vomiting and progressive abdominal distention.

Physical examination revealed an elderly, well developed but poorly nourished Caucasian female in moderately severe distress complaining of generalized abdominal pain. She was uncooperative, had poor skin turgor and was noted to have diminished urinary output. The heart and lungs were clear; the blood pressure was 120/80 mm. Hg and the pulse was 100. The abdomen was greatly distended and tympanitic, but not particularly tender. No discrete abdominal masses were present and rectal examination was negative. Occasional abortive peristaltic rushes and scattered high-pitched tinkling peristaltic sounds were heard. There were no external hernias or previous abdominal surgical scars.

The hemoglobin was 12 gm. per cent and the white blood count was 11,000 per cu. mm. with an essentially normal differential. The urine had a trace of albumin with a specific gravity of 1.020.

Scout roentgenograms of the abdomen showed an enormously distended gas-filled intestinal loop in the upper abdomen just to be left of the midline. In addition, there were numerous distended loops of small intestine. A barium enema examination showed obstruction of the barium in the mid-transverse colon with a definite spiral twist at this point. (Fig. 2.)

A diagnosis of volvulus of the right colon was made, and operation was performed after suitable preparation with parenteral fluids. At surgery there was volvulus of the entire right half of the colon located in the upper abdomen to the left of the midline. There was complete lack of fixation of the right colon to the posterior abdominal wall. The bowel was viable and, following detorsion, it was possible to demonstrate its remarkable hypermobility. The cecum was relocated in the right lower quadrant and secured to the anterolateral abdominal wall with a tube cecostomy. The patient's postoperative course was uneventful and the cecostomy tube was removed on the twelfth day. There was prompt spontaneous closure of the cecostomy fistula.

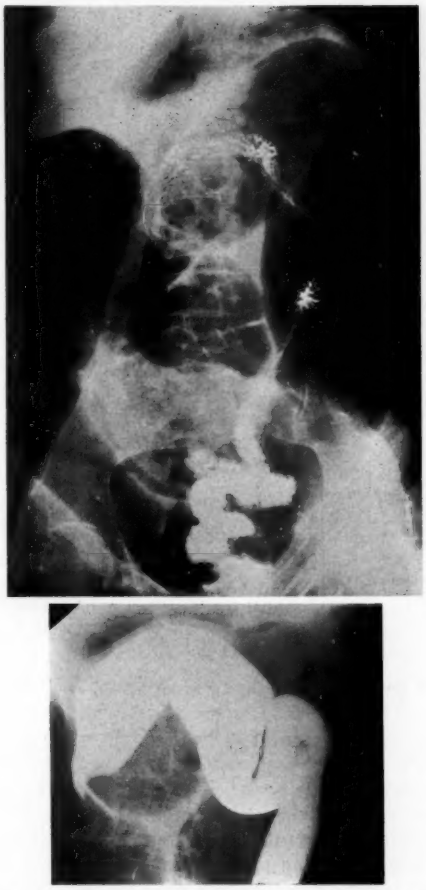
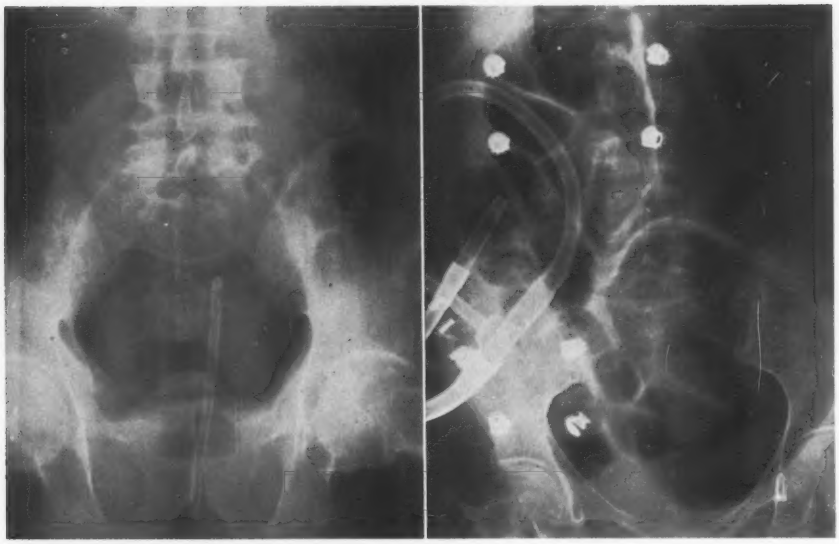


FIG. 2. Case 11. The roentgenogram on the top shows the extreme distention of the right colon while the film on the bottom demonstrates the point of obstruction and spiral twist present in the transverse colon.

ANALYSIS OF CASES

This is a study of fourteen consecutive verified (surgery or autopsy) cases dating from January, 1942 to December, 1958. Eight cases (57 per cent) were of the acute fulminating type and six (43 per cent) were of the acute obstructive variety. The over-all mortality was 35 per cent. The mortality in the acute fulminating type was 50 per cent and in the acute obstructive type it was 17 per cent. The sex distribution was equal with seven males and seven females. The average age was fifty-five years, ranging from fifteen to eighty-four years of age.



3 4

FIG. 3. This roentgenogram is from another case of cecal volvulus in which the distention is marked and the cecum is located in the pelvis.

FIG. 4. Roentgenogram shows marked distention of the ascending colon from volvulus.

The over-all incidence of gangrene was 64 per cent. In the acute fulminating type the incidence of gangrene was 75 per cent while in the acute obstructive group it was 33 per cent. It is important to note the close relationship between the presence of gangrenous bowel and the mortality rate. Gangrene of the bowel was present in all fatal cases, and this accounts for the high death rate of 50 per cent in the acute fulminating type. The high over-all incidence of gangrene (64 per cent) in the fourteen cases emphasizes the catastrophic nature of acute volvulus of the cecum and right colon. Four of the nine patients with non-viable bowel survived following right hemicolectomy. This demonstrates that patients with non-viable bowel can be successfully treated by prompt resection, if an early diagnosis is made. It is evident that any improvement in the survival rate in this condition must depend upon earlier diagnosis and prompt operation in the non-viable cases.

DIAGNOSIS

An understanding of the basic features of the two chief types is important in the early diagnosis of volvulus of the cecum or right colon. The acute fulminating type must be considered in the diagnosis of any acute catastrophic abdominal condition. There are no clinical findings which distinguish if from other serious conditions, but roentgenographic studies may be diagnostic. Fortunately, many of the diseases with which this fulminating variety is confused also demand early surgical exploration.

The clinical features of the acute obstructive type are suggestive of low or terminal small bowel obstruction. Small bowel obstructions are ordinarily due to band adhesions, hernias or various other causes, and are seldom associated with volvulus of the right colon. Distal small bowel obstruction secondary to volvulus of the cecum or right colon is an urgent surgical problem because colonic gangrene is relatively common even in this acute obstructive type.

Roentgenographic studies are essential in the diagnosis of volvulus of the cecum or right colon. The most typical finding on a scout roentgenogram of the abdomen is a greatly distended loop of cecum or right colon located in the middle or upper abdomen [1,4]. This dilated loop is sometimes situated in the pelvis. There is frequently an associated absence of the cecal gas pattern from the right

lower quadrant of the abdomen. If a barium enema is performed, a spiral twist may be seen at the site of the volvulus with obstruction to the further passage of barium. These various roentgenographic features are illustrated in Figures 3, 4 and 5.

In the acute fulminating type the roentgenographic findings are largely confined to the distended loop of cecum or right colon with minimal small bowel distention. However, in the acute obstructive variety a well developed pattern of distended small bowel is usually seen in addition to the dilated cecum or right colon. In acute fulminating cases the clinical course is so rapid that a well established small bowel obstruction pattern does not have time to develop, whereas in the acute obstructive type this may be such a salient feature that the volvulus itself is overlooked.

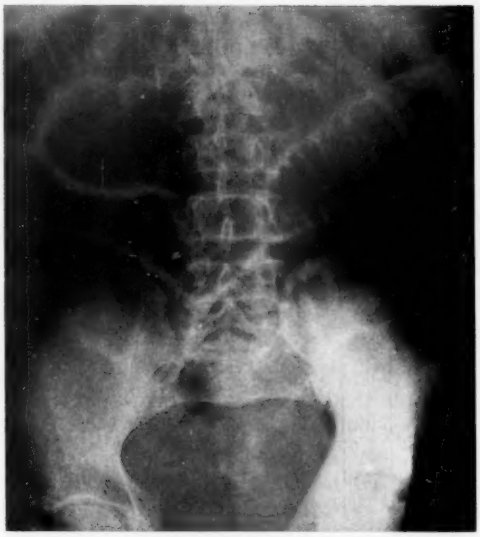


FIG. 5. Roentgenogram shows minimal evidence of volvulus of the right colon, but the small bowel obstruction pattern is prominent.

TREATMENT

Volvulus of the cecum or right colon demands early surgical intervention if treatment is to be successful. Right hemicolectomy is the treatment of choice when gangrenous changes are present. The only alternative procedure available is exteriorization of the right colon, and this is generally undesirable. Exteriorization cecostomy may be indicated in selected instances in which there is a small localized patch of cecal gangrene. Detorsion with fixation of the cecum in the right lower quadrant is indicated when the colon is viable. Tube cecostomy effectively accomplishes fixation and decompression of the dilated colonic segment. There appears to be no definite advantage of various cecopexy procedures over simple tube cecostomy for cecal fixation. Cecostomy should always accompany detorsion of a volvulus of the cecum or right colon, and if there is proper fixation of the cecum in the right lower quadrant, no recurrence should be expected. It is evident that right hemicolectomy will frequently be necessary in the acute fulminating type, while detorsion and cecostomy will often be indicated in the acute obstructive variety. The majority of patients with acute volvulus of the cecum or right colon require preoperative blood volume replacement. Hypovolemia and shock are especially common in the acute fulminating type with gangrene in which large quantities of blood are lost into the infarcted colon.

COMMENTS

Gangrene produced by volvulus of the cecum or right colon may result from either mesenteric vessel occlusion or from marked intracolonic pressure. Tight mesenteric twisting first occludes the venous return and later the arterial supply. Rotary mesenteric torsion with vascular occlusion results in early gangrene and the loss of large quantities of blood into the infarcted colonic segment. When volvulus produces predominately luminal obstruction, gangrene may be secondary to high intraluminal pressure. The marked intraluminal tension gradually occludes the intramural vessels producing ischemic necrosis, and this is particularly apt to be in the cecal area where the blood supply is relatively poor. Such segmental infarction and gangrene in the cecum may be followed by perforation with diffuse peritonitis. When there is luminal obstruction and competence of the ileocecal valve, the involved colonic segment becomes a closed loop greatly increasing the danger of distention, infarction and perforation. Regurgitation from the colon into the small bowel through an incompetent ileocecal valve provides some protection from gangrene and perforation. Another closed loop obstruction may be formed by inclusion of the terminal ileum in the volvulus.

The gangrenous changes appearing in the acute fulminating type are usually the result of mesenteric vessel occlusion from a tight, rapid twist. Occasionally in the fulminating type, if luminal obstruction predominates, a closed loop mechanism is probably present. These factors account for the sudden onset, rapid clinical course and high incidence of gangrene in this variety of volvulus. Luminal obstruction without any closed loop mechanism is more frequently seen in the acute obstructive type of volvulus of the right colon, although any of the situations producing bowel gangrene may be present.

The diagnosis of volvulus of the cecum is especially treacherous in patients who have had recent abdominal operations. If volvulus of the cecum or right colon is present, a roentgenogram may show the distended cecum to be in the epigastrium; this may be interpreted as gastric dilatation with a fatal delay in diagnosis. A "distended stomach" unrelieved by nasogastric suction, combined with an empty right lower quadrant, is suggestive of cecal volvulus. Volvulus of the cecum or right colon is also deceptive when it occurs as a postpartum complication. Volvulus of the right colon should be considered in patients with clinical and roentgenographic findings suggestive of low, small bowel obstruction, particularly in the absence of external hernias and abdominal scars. One must have an awareness of the varied clinical manifestations and interpret abdominal roentgenograms correctly in order to improve diagnostic accuracy in this condition.

It is of interest to note some of the differences between volvulus of the cecum or right colon and volvulus of the sigmoid. Right-sided volvulus is based on a failure of fixation with extreme hypermobility, whereas volvulus of the sigmoid is due to a redundant colon with a narrow base of attachment. This extreme hypermobility of the right colon favors rapid, tight mesenteric twisting resulting in a very high incidence of gangrene. It is likewise of interest that the over-all incidence of gangrene in this series was 64 per cent as compared with a 22 per cent incidence of gangrene in a recently published study of volvulus of the sigmoid [6]. Resectional therapy is only necessary for volvulus of the right colon when gangrenous changes are present, whereas definitive treatment for volvulus of the sigmoid requires ultimate resection of the redundant sigmoid loop. Both volvulus of the right colon and sigmoid have acute fulminating clinical types [6], although this variety is proportionately more common in the former group.

Two of the five deaths in this group of fourteen cases deserve special comment. One patient, seen early in the series with volvulus of the right colon, was inadequately managed. Volvulus was unsuspected until autopsy in the other instance, although review of the record suggests that the diagnosis possibly could have been made. Favorable results in these two cases would have substantially reduced the high over-all mortality rate. Sharp reduction in the mortality rate of patients with volvulus of the right colon should be possible by earlier diagnosis and prompt surgery.

SUMMARY AND CONCLUSIONS

A study of fourteen cases of acute volvulus of the cecum or right colon is presented. A clinical classification into two major types is proposed, the first being the acute fulminating type and the second the acute obstructive type. The acute fulminating variety of volvulus of the cecum or right colon is characterized by sudden onset, rapid clinical course, signs of peritoneal irritation and the early development of gangrene of the bowel. The acute obstructive type is chiefly characterized by its simulation of the clinical picture of low, small bowel obstruction.

Volvulus of the cecum or right colon is associated with a high incidence of gangrene of the bowel (64 per cent); this is especially true of the acute fulminating type. The mortality rate in this series was 35 per cent which parallels the incidence of intestinal gangrene. The basic cause of the volvulus is inadequate fixation of the right colon resulting in hypermobility. When volvulus occurs it produces varying degrees of luminal obstruction and mesenteric vessel occlusion, depending upon the rapidity and tightness of the twist.

Diagnosis is dependent upon an awareness of the disease with its clinical types and upon abdominal roentgenograms. The most important roentgenographic finding is a greatly distended loop of cecum or right colon located in the upper abdomen or pelvis.

Right hemicolectomy is the treatment of choice when there is gangrenous bowel. Detor-

sion with cecostomy is effective surgical management when the intestine is viable. Hypovolemic shock is frequently present and requires vigorous blood and fluid replacement.

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DISCUSSION

H. Rocke Robertson (Vancouver, B. C.): I have been most interested in this paper which prompted me to look up our cases of volvulus of the cecum. I was somewhat surprised to find that during the past few years we had twelve cases in which the diagnosis had been confirmed at operation without a doubt. For a glorious moment I thought we were going to have more cases than they were able to find at the Los Angeles County General Hospital, but I had to eliminate a number of the cases that had been listed as volvulus of the cecum for want of sufficient detail to justify the diagnosis.

In going over our twelve cases I found they did not all fit into the fulminating and acute obstructive classification that the authors mentioned. There were several that I would describe as being subacute, for the patients had moderately severe symtoms over a period of many days and yet were quite fit to withstand operation following admission. Our experience, I found, was very much the same as the authors'. Five of our twelve patients had been treated by resection of the right colon, and one died. Six were treated by reduction of the volvulus and caecostomy; of these, two died. In one patient, reduction of the volvulus was followed by fixation of the cecum to the anterior abdominal wall, with recovery.

I believe that this condition is a most treacherous one in two ways particularly. First, it is difficult to diagnose. In our series the radiological diagnosis was missed more often than it was made. The reason for an occasional miss was the presence of a huge gas-fluid level containing viscus in the left upper quadrant of the abdomen which anyone might mistake for the stomach. Actually, it proved to be the cecum, as the authors pointed out in one case. I think I am correct in stating that in none of our cases was a confident diagnosis of volvulus of the cecum made preoperatively, and in several I think the patient was watched for two or three days. As luck would have it, these patients all recovered.

The other respect in which volvulus of the cecum is treacherous, I think, is that it may mask some other condition. I know of three instances in which this has occurred. Once, while I was visiting another center where I was particularly keen that all should go well, I was assisting the resident operate upon what both he and I had agreed was a volvulus of the cecum. The patient was an elderly man who had undergone total prostatectomy ten days or so previously. He was quite ill with a distended and slightly tender abdomen, and his x-ray film showed a huge gas shadow in the right lower quadrant which, together with a tympanitic mass in that region, led us to the diagnosis. When his abdomen was opened, the diagnosis was confirmed and volvulus of the cecum was discovered and untwisted. The cecum was quite discolored and we were satisfied that it was giving rise to enough peritoneal irritation to explain the physical findings. Perfectly satisfied with our performance, we proceeded to close the abdomen. Trying to be helpful, I was retracting some loops of intestine into the patient's upper abdomen to provide exposure when I withdrew my hand momentarily and found some turbid bile dripping from the tips of my fingers. It occurred to me that something else might be amiss in the abdomen. It turned out that the patient had a perforated gallbladder as well which we had come within an ace of missing.

I was telling this story to a colleague a few weeks later and he stopped me at the point at which I began to tell of the dripping fingers to give me the diagnosis—perforated gallbladder. I asked him how he knew and he told me that he had had a similar experience a few days before.

The third instance in which I suspect that volvulus of the cecum was secondary to another serious condition appears in the series from our own hospital. One of our patients entered the hospital in critical condition. After a short period of attempted resuscitation, his abdomen was opened and a volvulus reduced. He died a few hours later and at autopsy was found to have a rupture of the lower third of the oesophagus with mediastinitis. From the postmortem findings, it would appear that the ruptured oesophagus had antedated the volvulus of the cecum. Thus, I think that volvulus of the cecum can be a secondary condition. Something causing peritoneal irritation and ileus occurs, and a

particularly mobile cecum may, as part of the process of ileus, become twisted to form a volvulus; this volvulus may then obscure the original condition. Hence, I would say that volvulus of the cecum can be very treacherous indeed.

DAVID METHENY (Seattle, Wash.): I would like to mention one small point of anatomy for I do not like to see what might be an error in anatomy perpetrated further in our records.

In the picture shown of the distended bowel with the small amount of gangrene on the side, the mesenteric border had the blood vessels coming in and entering the wall of the colon and then going around the entire circumference of the colon. That is not the way it occurs. About half the blood vessels enter the mesenteric border of the wall of the colon and anastomose, going each way. About another half of them go under the peritoneum to the taenia; this can be seen very frequently without difficulty if it is looked for. When these longer blood vessels reach the taenia they enter into the bowel wall and then divide and anastomose with those that are coming up from below, some anastomosing finally at the antimesenteric border.

This does have a little practical aspect because if in performing anastomosis you happen to pick off a long vessel which is bigger than usual, and then use that particular part of the bowel wall in the anastomosis, it may not be secure.

MATTHEW MCKIRDIE (Portland, Ore.): I would like to add one other facet to this very interesting picture that Dr. Hinshaw and his co-workers have presented. At Good Samaritan Hospital since 1951 we have had three patients with volvulus of the cecum and ascending colon. All were women, two in their thirties and one eighty-three years of age. The older woman required resection; the other two required derotation of the volvulus only. All patients made an uneventful recovery.

The point I should like to add is that the two younger women were pregnant at the time of the onset of the volvulus. One woman was twenty weeks pregnant and the other thirty-six weeks. The latter patient had a typical volvulus. A low cesarean section was performed and a live infant was delivered. The volvulus was successfully derotated.

The other patient had a typical picture of a long redundant ascending colon and about 270 degrees' rotation in a clockwise direction of the cecum and ascending colon. Following derotation she delivered a full term infant some sixteen weeks later.

I would like to ask Dr. Hinshaw if he will discuss the association of pregnancy with this condition from his review of the literature.

JOHN W. CLINE (San Francisco, Calif.): I have enjoyed this paper a great deal and would like to mention briefly seven cases of volvulus which I have personally treated over the last thirty years. All were clockwise in nature. Three of them occurred postoperatively and four were spontaneous. Four were of the obstructive type and three of the fulminating type. Three were treated by resection and four by tube cecostomy, with two deaths in the former group and one death in the latter. The deaths were all due to infection.

I am surprised the authors did not comment on the fact that derotation may be extremely difficult, and that one must decompress a colon which is grossly distended prior to attempting derotation.

One of the deaths in my series resulted from an error in judgment in an effort to reduce the volvulus without having previously decompressed the cecum.

I am surprised also that there was no mention of the fact that the terminal ileum usually is not attached to the posterior parietal peritoneum as well as the cecum and part or all of the ascending colon. The basic abnormality results from lack of fusion of the viscera to the parietal peritoneum.

DONALD T. HALL (Seattle, Wash.): I think Dr. Hinshaw and his group have given us a fine presentation of the clinical portion of this disease, but I have been quite interested in the eitiological aspects about which they said, I think, relatively little.

I am very much impressed with the similarity of this disease to congenital mid-gut volvulus in the newborn. In that particular disease, as you know, the rotation one finds is primarily what produces the clinical symptomatology, but basically the causal situation is that failure of fusion of the mesenteries is such that the entire mid-intestinal segment is suspended on the superior mesentery vessels which leaves it completely free to rotate.

I would like to ask Dr. Hinshaw if he has any further comments on the relationship of the mesenteric fusion in the patients he has seen. We know that in performing appendectomies there is a great deal of variability insofar as the mobility of the cecum is concerned. I think that volvulus of the cecum in those cases in which the mesentery is short is almost unheard of.

The other extreme, of course, is when there is complete absence of fusion of the mesenteries.

The thing that interests me is that if this assumption is correct, what is the precipitating factor that produces a volvulus of this sort when the potential has been present for many years without producing any difficulty?

A number of years ago I saw a patient in his mid-seventies who was in a completely moribund state with obvious intestinal obstruction. He died before we could get him to surgery. Autopsy showed a complete volvulus of the cecum with gangrene. On going over the history we learned from the patient's family that he had had recurrent

episodes of severe abdominal colicky pain from the time he was a very small child, indicating that there had been a fusion failure of his mesenteries with a recurring volvulus up to the time he reached his mid-seventies.

I think it is somewhat similar in analogy to an inguinal hernia where the sac is potentially present yet the hernia does not appear until later in life.

I would like to ask Dr. Hinshaw if he has any idea in his cases as to what might have been the precipitating factors in an abnormality which is basically one of congenital origin?

Carl P. Schlicke (Spokane, Wash.): The photograph that impressed me most was the same one Dr. Metheny commented upon, the tremendously dilated bowel with the beginning impairment of circulation. I marvel at the fortitude of the person who would fill that bowel with barium. I wonder what additional information would be obtained which would justify the added risk of pouring a radiopaque medium of that type into a bowel which is already distended and in many cases gangrenous.

Several years ago we reviewed a number of cases of intestinal obstruction at the Mayo Clinic. There was a very significant increase in morbidity and mortality among those patients who had had barium studies, not only those who inadvertently were given barium from above but also those receiving it by rectum. Even in the absence of perforation, such studies added greatly to the whole problem. I think that if sufficient information could be obtained from the x-ray films, I would certainly question the advisability of adding a barium enema to the study.

Wm. F. Pollock (San Monica, Calif.): In very young children the appendix has a base which is proportionately broader than it is in the older child. We have seen one case of this disease in a child in whom the appendix showed evidence of acute inflammation. This will serve to call attention to a technical maneuver that might be helpful. One can use the appendix as the point of introduction of the tube cecostomy. It is feasible to perform appendicostomy for a tube cecostomy since the appendix must be considered in the treatment of this disorder.

Leon Goldman (San Francisco, Calif.): May I ask one question? We have encountered patients with volvulus in whom we have not found any dilatation of the small bowel either during roentgenologic examination or at the operating table although complete intestinal obstruction was present.

If the authors have any explanation for the lack of dilatation in some of these patients I would like to hear about it.

David B. Hinshaw (closing): We are pleased by all these excellent comments, and I will try to answer the questions.

Our cases actually represent about half the cases at the Los Angeles County Hospital. They are drawn only from the Surgical Service of the College of Medical Evangelists, and if the whole hospital were to be included this number would be at least doubled.

We were especially grateful for Dr. Robertson's comments, particularly those about the acute underlying conditions which are sometimes found.

Dr. McKirdie called attention to the association of this disease with pregnancy. We have read about this but did not happen to have such a case in our group.

The problem of anatomy mentioned by Dr. Metheny is interesting. We agree with him completely, but perhaps our photograph is not clear.

We appreciate Dr. Cline drawing attention to decompression prior to detorsion. We have likewise found that this is frequently necessary.

The term volvulus of the cecum is, of course, a misnomer because the lack of mesenteric fusion usually, but not always, involves the entire right half of the colon. This lack of fusion also includes the terminal ileum in many cases. We appreciate Dr. Hall re-emphasizing this point.

Dr. Schlicke mentioned the dangers of barium enema in these circumstances. We do not recommend this except in the occasional case in which the scout roentgenogram is very equivocal. If the diagnosis is in doubt, I think a barium enema examination can be made if the radiologist is gentle.

Dr. Pollock emphasized appendicostomy. Several of our patients were actually treated this way.

Dr. Goldman called attention to the problem of the lack of small bowel distention in these cases. We are not prepared to explain this except to note that this was sometimes the situation. In those cases with very rapid clinical courses in which the patient had a gangrenous cecum or right colon, we assumed that there was not enough time for prominent small bowel distention to develop.

Biopsy with Delayed Radical Mastectomy for Carcinoma of the Breast

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THE procedure of biopsy as a diagnostic aid in surgery was first established by Virchow [9] in 1854. The procedure of frozen section in biopsy work owes its existence largely to L. B. Wilson [10], a pathologist at St. Mary's Hospital in Rochester, Minnesota. In 1905 he described his rapid method of preparing fresh tissues for the microscope in a half page article in the *Journal of the American Medical Association*. With a few changes it is much the same method that is in general use today. It has been assumed that immediate radical surgery is preferable if the diagnosis is certain. Trained pathologists have developed a high degree of skill in interpreting frozen sections. Pitts, Sturdy and Coady [6], report 326 accurate diagnoses on frozen section out of 327 tumors of the breast examined. The three hundred twenty-seventh specimen was deferred for hematoxylin and eosin staining and was found to be benign. This is in contrast to Bloodgood's [1] report of twenty-four years ago, at which time he frequently sent sections or pieces of tissue to two or more pathologists to confirm his diagnosis. He was of the opinion that delay did no harm if postbiopsy radiation was given in the interval.

The literature contains contradicting opinions on the subject of delay between biopsy and definitive surgery in carcinoma of the breast.

Ewing [2] believed that the surgeon should not remove a tumor nodule from a breast except in the operating room where he is prepared to have an immediate diagnosis made and a proper operation performed. In his opinion, the drawbacks of delayed surgery were as follows. (1) Mechanical trauma dislodges cancer cells and cuts across cancerous lymph nodes. (2) Delay gives the dislodged cells opportunity to reach distant lymph nodes. (3) Subsequent hyperemia may stimulate growth of the cancer.

Harrington [3] did not believe it was ever justifiable to remove any growth from the breast without immediate microscopic examination of the frozen sections and immediate suitable surgery.

On the other hand, McGraw and Hartman [4] stated that there may be a limited place for delayed biopsy. Haagensen [11] reported a total of forty-nine cases in which there was an interval of more than seven days between biopsy and operation with a five-year clinical cure rate exceeding that of 492 cases of biopsy at operation. His explanation was that diagnostic difficulties requiring delay are more frequent with well differentiated tumors that are as a group less malignant.

Siemens [8] reported a delay of ten to fourteen days between biopsy and radical operation in fifty-three of his patients, but with a comparatively high cure rate. Scheel [7] reported that biopsy carried out one to several days before radical operation had no untoward effects upon the cure rate in a series of 112 cases of excision biopsy, but he gives no detailed figures.

Pierce, Clagett, McDonald and Gage [5] traced the records of ninety-five patients with a delay of four days to two years and three months between biopsy of the breast and surgery. All the delayed radical mastectomies were performed at the Mayo Clinic. There was a five-year survival rate of 61.1 per cent. A control group of 554 patients who underwent immediate radical mastectomy at the Mayo Clinic had a five-year survival rate of 60.1 per cent.

At the present time, at least in British Columbia, the supply of trained pathologists is failing to keep pace with the supply of trained

TABLE I
DISTRIBUTION OF PATIENTS BY LOCATION OF LESION

Location	No. of Patients (51)	Percentage
Upper outer	23	45.0
Lower outer	5	9.8
Upper inner	5	9.8
Lower inner	2	3.9
Central	5	9.8
"Lateral"	2	3.9
Extensive	2	3.9
Not noted	7	14.0

surgeons. As a result, many towns and small cities over the Province have trained surgeons and adequate operating facilities but no pathologist immediately available. Thus the question arises and is frequently asked at seminars on surgery of the breast, "Is any harm done the patient in performing radical mastectomy some days after the biopsy?"

Our material consists of fifty-one biopsy specimens of the breast received at St. Paul's Hospital from thirty-four surgeons in the years 1948 to 1952 inclusive, with a follow-up on the delayed radical operations and the survival rate from five to ten years. Over 100 specimens were received during this period but only fifty-one could be traced satisfactorily.

It will be noted in Table I, that 45 per cent of the lesions were in the upper outer quadrant and 23 per cent were located centrally or in the inner quadrants.

As Table II indicates, the excisional type of biopsy makes up 76.3 per cent of the total. No

TABLE II
TYPES OF BIOPSY AND OPERATION

	No. of Patients	Percentage
Type of biopsy (51 patients):		
Incisional	8	15.7
Excisional	39	76.3
Simple mastectomy	1	2
Biopsy of the axillary node	1	2
Not specified	2	4
Type of operation (51 patients):		
Radical	47	92
Simple	4	8

TABLE III
INTERVAL BETWEEN BIOPSY AND MAJOR OPERATION*

Interval (days)	No. of Patients (51)	Percentage
2 to 5	4	7.8
6 to 12	22	43.1
13 to 21	18	35.3
22 to 35	2	4
39 to 145	5	9.8

* Average delay, 18.4 days.

needle or aspiration biopsies were performed. The only simple mastectomy was performed as a biopsy procedure, followed by radical operation seven days later. Biopsy of the axillary node was performed in the only case of carcinoma in a pregnant woman in the series, a large medullary carcinoma.

Ninety-two per cent, or forty-seven patients had radical operations, described as "radical Halsted," "radical Rodman," or simply radical. Only four patients underwent simple mastectomy. Three of these were living and well from seven to ten years.

In Table III it is seen that the delay varied from two to 145 days; in forty-four cases, or 86.2 per cent the delay was twenty-one days or less. The average delay was 18.4 days.

Table IV indicates the pathologic conditions found. Clinical staging with any accuracy was impossible in these cases. However, the presence or absence of axillary nodes was considered.

It will be noted in Table V that eighteen patients, or 35.3 per cent had positive axillary nodes, based on pathological examination of the radical specimen later received. Seventeen pa-

TABLE IV
PATHOLOGY

Pathologic Condition	No. of Patients (51)	Percentage
Scirrhus	24	47
Carcinoma simplex	9	17.6
Intraductal carcinoma	7	13.7
Adenocarcinoma	3	5.9
Medullary carcinoma	2*	4
Colloid carcinoma	1	2
Not classified	5	9.8

* One case of carcinoma in a pregnant woman.

TABLE V
AXILLARY NODES

	No. of Patients	Percentage
Positive	18	35.3
Negative	17	33.3
Not classified	16	31.4

tients, or 33.3 per cent showed no involved axillary nodes. Sixteen were not classified. In many of these sixteen cases the radical specimens were not received.

The over-all survival rate of this group of patients was somewhat surprising. (Table VI.) It will be noted that 62.7 per cent of the entire group survived five or more years (actually six or more years). Of forty patients operated upon, twenty-four or 60 per cent survived seven or more years. Fourteen of twenty-seven patients operated upon, or 51.8 per cent, survived eight or more years, 53.3 per cent of fifteen patients operated upon survived nine or more years, and four of six, or 66.6 per cent, are living and symptom free at the end of ten years.

It would be impossible to run a control series on this group because of the wide variation in operating conditions. However, a comparison with some of the large standard series of survival rates may be of interest. (Table VII.)

Thus our small series compares favorably with these larger series.

An analysis of tumor size shows pathologists' dimensions recorded in thirty-seven specimens of excision biopsy. The average size was 2.2 cm.

The largest tumor recorded was 7 cm. Fourteen of the aforementioned thirty-seven patients had tumors varying from 2.5 to 7 cm., with an average size of 3.4 cm. Of these patients, 50 per cent survived six to ten years.

The recorded measurements would indicate that as a rule the tumors were excised while of relatively small size. One may postulate that this group of carcinomas of the breast represents a relatively early stage of the disease, although 35 per cent of the patients had proved axillary metastases.

TABLE VI
OVER-ALL SURVIVAL RATE

Time (yr.)	No. of Patients	Percentage
5 or more	32 (of 51)	62.7*
6 or more	.....	62.7
7 or more	24 (of 40)	60
8 or more	14 (of 27)	51.8
9 or more	8 (of 15)	53.3 living and well
10	4 (of 6)	66.6 living and well

* These patients actually survived six or more years.

TABLE VII
FIVE-YEAR CLINICAL CURE RATES

Series	No. of Cases	Five-Year Clinical Cures (%)
Presbyterian Hospital	492	51
Haagensen [11]	202	56.7
Mayo Clinic	554	60.1
University of Chicago	186	54.3
Present series	51	62.7

SUMMARY

In this small series of cases in which fifty-one biopsy specimens were received, and mastectomy was performed on the average of 18.4 days later, we have shown an over-all survival rate of 62.7 per cent of five-year cures.

While we would not go on record as advising delay in radical mastectomy, we have been unable to demonstrate in this series that any harmful effects result from excision biopsy of small tumors with delay of a few days for definitive treatment while a pathological diagnosis is being made.

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DISCUSSION

ROBERT E. MCKECHNIE (Vancouver, B. C.): Dr. Jackson has presented a paper that represents considerable work and effort and the figures from British Columbia that he has obtained are comparable to studies made elsewhere. These figures are probably only of academic interest to surgeons working with adequate hospital and pathological facilities around them and that is as it should be, inasmuch as biopsy followed by immediate radical mastectomy is the ideal procedure in carcinoma of the breast. However, where surgeons are working under circumstances that do not allow immediate frozen section studies of excised tumors of the breast, those figures presented by Dr. Jackson are of great interest.

Speaking in reference primarily to surgeons from British Columbia it must be noted that there are only four communities in the province in which pathological facilities are available. The import of this is realized when one recognizes that the area of British Columbia is greater than the combined area of the states of Washington, Oregon and California. The surgeon in the pathological hinterland of British Columbia when faced with a small clinically undiagnosable lesion of the breast must decide without help what to do with it. He can send the patient to a center for biopsy followed by immediate surgery if indicated. This he quickly finds out is an unwieldy and unpopular method of handling the situation as 80 per cent of such small lesions usually prove to be benign. Thus eight out of ten of his patients have had at times to travel great distances with consequent expense and inconvenience to find the lesion was a simple one. In a small town this method of approach is dropped by common consent. The surgeon may choose to observe the tumor assuming the calculated hazards of delay and the possibility of the dissemination of cancer cells by repeated palpation. The third method of complete excision of the growth with delayed radical mastectomy usually is his treatment of choice and Dr. Jackson's study seems to bear out that the risk is not unjustifiable.

From another point of view, namely the care of carcinoma of the breast, this type of procedure may be villified under the circumstances just described. The methods of treating carcinoma of the breast are many and controversial. The surgical, radiation and hormonal attacks are well known and at times highly unsuccessful. One method of attack that is best recognized as successful is to perform a biopsy on the early lesion. I believe that early biopsy of an early lesion is the best single method of increasing the survival rates of patients with carcinoma of the breast.

May I point up this opinion by citing from my series one case of biopsy followed by delayed radical mastectomy? This thin-breasted woman had a tiny nodule in her breast and I had routinely advised her to undergo biopsy. She pleaded family and economic responsibilities that prevented her staying in town for the inevitable delay and expense associated with hospitalization and frozen section studies of the tumor. Being moved by her pleadings I had two other surgeons see the patient and was assured the lesion was undoubtedly benign and I was worrying unnecessarily. To compromise with my conscience I removed the tumor under local anaesthesia in the office only to find later that the tumor was malignant. Radical mastectomy was carried out and I like to think that that woman is alive twelve years later because the tumor was discovered early in its career.

MARTIN A. HOWARD (Portland, Ore.): Our pathological department at Good Samaritan Hospital deals with both immediate and delayed mastectomy. All the surgeons at Good Samaritan Hospital with occasional exceptions perform radical mastectomy immediately following the diagnosis on frozen section of carcinoma of the breast.

Of the many biopsy specimens of the breast which are sent in from outlying hospitals each year there are only about twelve a year which indicate carcinoma. There are about four operations that, for one reason or another, our own staff postpones, or a few more occasionally, for various reasons. Usually they are not sure of the diagnosis following the frozen section for carcinoma.

These patients are operated upon from one to two weeks following the biopsy of the breast. Our pathological department believes that a very careful, gentle biopsy with delayed radical mastectomy is probably less harmful than an examination in the breast unless the examination has been carried out with considerable care. There is some belief that it is much safer to perform an excision of the tumor for biopsy than it is to perform an incisional biopsy, if radical mastectomy is to be delayed. In this series most of those procedures performed were excision biopsies.

Now I think that most of us in our hospital, if we are quite sure that we are dealing with carcinoma, perform incisional biopsy at the time rather than excisional biopsy.

Haagenson and Stout show that the results of delayed radical mastectomy are not quite as good as

INFLUENCE OF BIOPSY ON RESULTS OF RADICAL MASTECTOMY*

Procedure	No. of Cases	Local Recurrence		Five-year Cures	
		No.	Per cent	No.	Per cent
No biopsy	106	7	6.6	65	61.3
Biopsy some days before operation	11	3	27.3	5	45.5
Biopsy at operation	114	13	11.4	74	64.9
Total	231	23	10.0	144	62.3

* Cases operable according to our criteria and without metastases to the axillary lymph nodes.

are the immediate results (See Table). This, of course, is a very small series of cases, and as Drs. Jackson and Pitts have stated, in one series Dr. Haagensen believes that the results are just as good.

In the first series there were about 7 per cent local recurrences and the five-year cures were 61 per cent. For biopsy with some delay (only eleven cases) there were 27 per cent local recurrences and 46 per cent five-year cures. Biopsy followed by immediate operation resulted in 11 per cent local recurrence and 65 per cent five-year cures.

Recently Haagensen has used triple biopsy for the diagnosis of carcinoma in regional lymph nodes. From three to seven days later radical mastectomy is performed if the results are negative. He believes that these triple biopsies save his patients from futile radical mastectomies. He does not believe that the delay adds, and I quote, "appreciably to the danger of distant metastases."

It is our belief, however, at Good Samaritan Hospital that, everything else being equal, immediate radical mastectomy following diagnosis on frozen section is certainly much less traumatic to the patient emotionally, and we feel rather strongly that the long term results are better.

H. Glenn Bell (San Francisco, Calif.): I have been interested in this subject for some time, and seeing this program I thought of comparing our own experience with Drs. Jackson and Pitts' report. It is very interesting that our figures come out very much the same. We have had 115 patients who fit into the group described by Drs. Jackson and Pitts in which biopsy was performed elsewhere, and the patients were referred to us anywhere from two days to two weeks afterwards. In that group the five-year survival rate was 58 per cent and the ten-year survival rate was 42 per cent, which would fit very well with his group. Those are the patients in stage I and stage II. In the routine cases that we have handled at the Medical Center, approximately 1,000 cases, in which we have performed the biopsies ourselves and then proceeded with the radical mastectomies, the five-year over-all survival rate was 61 per cent and the ten-year survival rate rate was 41.8 per cent, so that the difference is extremely small. I personally thought it would be much larger than that. I still believe that the radical procedure should immediately follow biopsy.

I realize that British Columbia is a large area, but I was somewhat disturbed as no one had made any suggestion or laid down any rule that I know of that says a surgeon cannot go to the laboratory and look through a microscope. I still see frozen sections from my patients. Perhaps I do that just because I am old-fashioned. We have good pathologists and I depend upon them, but I still like to see these frozen sections; it is a rare exception, but one which we do find once or twice a year, when both the pathologist and I cannot be certain whether we are dealing with a malignancy or not. In this case we postpone the procedure, and in twenty-four hours have our routine section.

Some doctors, I think, know that I still can cut a frozen section if I have to and stain it and make my diagnosis and then perform radical mastectomy.

Hebert W. Meyer (New York, N. Y.): I think we are all extremely grateful to Drs. Jackson and Pitts for bringing forward this very important and interesting subject, for which there is not as yet a definite answer. There is no question but that biopsy is of great importance in determining what should be done for these poor women with tumors in their breasts.

As far as aspiration biopsy is concerned it is employed in those clinics in which are seen tremendous numbers of patients, as for instance the Memorial Cancer Center in New York. Time makes it necessary to perform biopsies and await the report. Even if frozen sections are taken, schedules are crowded with so many operations that frequently biopsy is performed in the morning and if the results are positive the radical operation is carried out in the afternoon but not immediately.

Dr. Farrell was asked at one of the meetings of the Ewing Society whether he thought there was any importance in the interval between biopsy and radical operation, and it was his opinion that the shorter the interval the better for the patient.

As far as incisional biopsy is concerned I believe it may be performed if the tumor is a large one. To incise the tumor and take a piece out is a perfectly correct procedure. Haagensen does so in almost every instance. However, I have had the personal experience of operating upon three patients for whom good surgeons had performed what they thought was incisional biopsy and had never gotten

down to the tumor which in each case was a small one. They had only removed some infiltrated fat or breast tissue near the tumor. Therefore, I believe there is no question but that the excisional biopsy is by far the best.

The one important point is that no matter what we do for carcinoma of the breast, as Dr. Howard has so beautifully brought forward, it must be done with gentleness, gentleness in handling tissues, gentleness in touch, and that applies also to the physical examination as well as the prepartion of the operative field. I have seen nurses in an operating room when I was not the operating surgeon, prepare a breast in such a way that I was horrified because I could imagine those tumor cells being spread by embolism by the rough rubbing over the breast and the spreading of the disease. Unfortunately we have no way of knowing at the present moment whether when we operate upon the patient there are any microscopic tumor cells distant in the body at the time of operation that will bring about a poor result for radical mastectomy. Some day we will be able to diagnose those early distant metastases.

In 1956 at the meeting of the Western Surgical Association, Drs. John B. Davis of Omaha and Warren Cole of Chicago presented a paper (published in the *Arcbives of Surgery*) in which they provided some very interesting statistics showing that in their opinion the shorter the delay between biopsy and operation the better for the patient. Dr. Cole even made the statement in the discussion of the paper that many surgeons who are proficient in gross pathology will not necessarily wait for the pathological report but will proceed with radical mastectomy without a positive microscopic report, depending on their gross pathological inspection.

PAUL P. JACKSON: I would like very sincerely to thank all the discussers of this paper. A paper like this immediately poses certain problems. At our own hospital in Vancouver we have a rule that nobody is allowed to perform biopsies on the breast unless he is qualified to proceed and perform a radical operation immediately. In other words, nobody is allowed to perform biopsy on the breast and have a surgeon stand by and wait to take over.

When these figures or any similar figures are published undoubtedly certain men in outlying districts will be quite interested and there is always a possibility that they might abuse these findings by removing tumors that should not be removed with delay, so I would like to stress in closing the importance in my opinion of using this sort of procedure only for very small tumors and those tumors in which the surgeon might believe there is an excellent chance of them being benign.

Cancer of the Thyroid

A TWENTY-YEAR FOLLOW-UP

JOSEPH W. NADAL, M.D., *Portland, Oregon*

THIS study is limited to patients with cancer of the thyroid who were treated over twenty years ago. It deals only with thirty-one patients in whom the diagnosis of cancer could be verified by modern criteria. Although the series is small, it is unusual in that a complete follow-up was obtained on every patient.

The cases used in this study were selected from the records of all patients who had had thyroid operations at The Portland Clinic prior to 1939. This covered the years 1916 through 1938, and involved 3,707 thyroid operations on 3,602 patients. Nearly all of these operations were performed by the late Dr. Thomas M. Joyce. The records were examined of all patients in whom the diagnosis of cancer of the thyroid had been made or suspected by the surgeon or pathologist, or in whom the diagnosis was suspected on the basis of the subsequent course of events.

Pathologic Classification. In all but a few cases the original microsections were located and re-examined during 1958. We were able to verify the diagnosis of cancer of the thyroid in thirty-one patients. Their lesions were classified as follows: papillary, thirteen; follicular, eight; undifferentiated, six; Hürthle cell, one; and unclassified, three.

No cases of "adenoma malignum" were included.

Treatment. The operative procedures performed at the time of diagnosis were: bilateral subtotal thyroidectomy, twenty-seven patients; total thyroidectomy, two; tracheostomy, one; removal of tissue for biopsy, one. During the years represented by this study, prophylactic neck dissections for cancer of the thyroid were not being performed in the Clinic.

Nineteen patients were given postoperative radiation therapy. Seventeen had radium, and two x-ray.

Previous Operations on Thyroid. Two patients had had thyroidectomies three and four years, respectively, prior to the operation at which cancer was discovered. It is suspected that cancer was present in each instance at the time of the first operation but this could not be proved. Both patients died of recurrent disease.

Secondary Operations for Cancer of the Thyroid. In six patients recurrent or persistent carcinoma in the neck, lymph nodes, thyroid gland remnant or scar made secondary operations necessary from three months to six years after the diagnosis. All six patients died of cancer, although one lived twenty-three years.

FOLLOW-UP STUDY

Contact was established with the living patients and with the Bureau of Vital Statistics, as indicated. All the patients were traced. The results of the follow-up study are summarized in Table 1. There were no operative deaths.

TABLE 1
RESULTS OF FOLLOW-UP STUDY OF CARCINOMA OF THYROID TWENTY-ONE TO THIRTY-TWO YEARS POSTOPERATIVELY

Histologic Classification	No. of Patients	Died of		Alive and Well
		Cancer of Thyroid	Other Causes	
Papillary carcinoma	13	2	5	6
Follicular carcinoma	8	2	5	1
Undifferentiated	6	6	0	0
Hürthle cell	1	1	0	0
Unclassified	3	2	1	0
Totals	31	13	11	7

TABLE II
PAPILLARY CARCINOMA: DEATHS DUE TO DISEASE

Patient No., Sex and Age	Comments
25600, F, 54...	1929: Resection of right lobe and isthmus for "benign goiter" 1932: Resection of "recurrent goiter" on right side; microsection showed highly anaplastic area, like sarcoma, and papillary area; radium therapy given 1933: Recurrent carcinoma in scar; patient died same year; autopsy showed growth in esophagus with area of squamous cell metaplasia
53560, F, 62...	1936: Bilateral subtotal thyroidectomy followed by radium therapy; ten months later metastatic nodes resected in right submaxillary region; five additional courses of radium therapy given during following four years 1941: Died five years after operation

TABLE III
PAPILLARY CARCINOMA: DEATHS DUE TO OTHER CAUSES

Patient No., Sex and Age	Cause of Death	Postoperative Survival (yr.)	Age at Death (yr.)
1561, F, 50...	Cardiovascular accident	30	80
4866, F, 51...	Arteriosclerosis	8	60
5044, F, 48...	Fell out of bed	28	77
33315, M, 51.	Hypertensive cardiovascular disease	26	77
61305, F, 45..	Carcinoma of cervix	12	57

TABLE IV
PAPILLARY CARCINOMA: PATIENTS LIVING AND WELL

Patient No., Sex and Age	Postoperative Survival (yr.)	Present Age (yr.)
10899, F, 30.....	32	62
23359, F, 38.....	29	67
39392, F, 52.....	26	79
57583, F, 46.....	21	67
61686, F, 32.....	21	53
66716, F, 40.....	20	60

Papillary Carcinoma. Of the thirteen patients with papillary carcinoma, two died of their disease. (Table II.) Five patients died of other causes eight to thirty years later. (Table III.) Their ages at death were fifty-seven, sixty, seventy-seven, seventy-seven, and eighty years, respectively. Six patients are still living and free of disease twenty to thirty-two years later. (Table IV.) The present ages of the patients still living are fifty-three, sixty, sixty-two, sixty-seven, sixty-seven. and seventy-nine years, respectively.

None of the thirteen patients were given what would today be considered adequate treatment. Only two underwent total thyroidectomy; the others had subtotal or partial thyroidectomy. Eleven received postoperative radiation to the neck, radium being used in nine patients and x-ray in two. None of the patients underwent neck dissection. It seems probable that at least one of the two patients who died of the disease might have been saved had neck dissection been performed at the time of thyroidectomy or soon afterward.

Undifferentiated Carcinoma. All six patients with undifferentiated carcinoma died within one year. Operation had apparently accomplished little more than provide tissue for biopsy.

Follicular Carinoma. Of the eight patients with a follicular type of carcinoma, two died of their cancer in nine years or less. Five others are dead and are known to have died of causes other than cancer of the thyroid. One is still living twenty-six years after operation.

Hürtble Cell Carcinoma. Only one patient had this type of cancer. She had undergone bilateral subtotal thyroidectomy in 1928. Microsections were reported as showing "malignant adenoma of low grade." However, in 1934, six years later, she had an operation for removal of a mass of recurrent cancer from the left side of her neck. In 1937 radium was applied to the same area, and in 1939 another operation was performed for removal of a mass of nodes on the left side of the neck. She died in 1952 of massive cancer in the same area, twenty-three and a half years after the original operation. It seems likely that an early neck dissection might have prevented the recurrence.

Unclassified Carcinoma. The three cases of unclassified carcinoma are so designated for

various reasons. In one case no tissue was obtained for biopsy, only tracheostomy was performed. In the other patients we were unable to locate the original slide, yet there was no reasonable doubt the patients had cancer of the thyroid. Two of the three patients died of their cancer within one year. The third died twenty-one years later (at the age of eighty-five) of heart disease.

COMMENTS

It was surprising to find only thirty-one instances of verifiable carcinoma in 3,602 patients having thyroid operations, an incidence of 0.86 per cent. Of course, it is probable that a few of the patients, who were eliminated from the study because we were not able to verify the diagnosis, did actually have carcinoma of the thyroid. (Incidentally, if they had been included the effect would have been to increase the percentage of apparent cures.) Also, it is possible a few records could have been lost or otherwise missed, although we made every effort to find them all.

One wonders whether the patients subjected to thyroid operations during these years and in this clinic were a truly representative sample of the goitrous population. In the earlier years of the study there was in this region probably a considerable backlog of persons with untreated goiters. Perhaps some of the patients with cancer had already been eliminated from the series by dying from the disease, leaving the patients with benign goiters for Dr. Joyce.

There is also the fact that from 1923 on there has been an actual or apparent increase in the incidence of cancer of the thyroid in each decade. Foss [2] in 1938 averaged the incidence in the reports of eleven authors and obtained a figure of 2.37 per cent. Hershey [4] reported an incidence of 1.6 per cent (in nodular goiter) in the period from 1930 to 1944, and 2.9 per cent in the period from 1945 to 1956. A study by Shallow et al. [5] indicated an increased incidence from 2.2 per cent to 6.8 per cent in two decades.

No attempt will be made to draw any firm conclusions from this study of only thirty-one patients. Certainly a statistical analysis would mean little. In general, the diagnostic groupings and the survival percentages are compatible with those reported in larger series.

Our high cure rate in the thirteen patients with papillary carcinoma may well be due to sampling error. In most studies of papillary carcinoma the incidence of regional lymph node metastases is greater than 50 per cent. Frazell and Foote [3] reported an incidence of positive nodes of 61 per cent, even when the nodes were clinically normal. Therefore, since our patients, operated upon over twenty years ago, did not even undergo neck dissection, it seems unlikely that half of them could have had cervical lymph node metastases and at the same time that eleven of the thirteen could live from eight to thirty-two years without evidence of recurrence ever developing. In this connection, it is interesting to see that Beahrs and Woolner of the Mayo Clinic [1] recently reported a fifteen-year follow-up on a group of fifty-seven patients treated for papillary carcinoma. Of forty-nine patients traced, thirty-seven survived (i.e., 75 per cent of those traced, or 65 per cent of the group).

In view of the actual results of the long term follow-up studies here and elsewhere, perhaps our present policy of performing neck dissections in most patients with papillary carcinoma of the thyroid should be modified.

The details of the radiation therapy employed were discussed with several radiologists. It appears that the amounts of radiation delivered were probably not sufficient to destroy metastatic carcinoma in the cervical lymph nodes. We believe it had no significant effect on the end results.

SUMMARY

Of 3,602 patients having thyroid operations at The Portland Clinic prior to 1939, thirty-one had verified cancers. A complete follow-up has been obtained on all thirty-one patients.

Treatment in twenty-seven instances was partial or subtotal thyroidectomy, and in two instances total thyroidectomy. Radium or x-ray therapy was frequently used postoperatively.

As would be expected, the thirteen patients treated for papillary carcinoma had the best outcome. Of these, eleven appear to have been cured, either having died of unrelated causes many years later (five patients) or being alive today, twenty-one to thirty-two years after their operations (six patients).

In contrast, all six patients with undifferentiated type of cancer died within one year.

In the entire group of thirty-one patients,

eighteen appear to have been cured of their disease.

There was no evidence that the postoperative radiation therapy employed altered the end results.

Acknowledgment: Dr. Frank Menne and Dr. Joseph Nolgren, pathologists at St. Vincent Hospital in Portland, Oregon, re-examined the microsections of the patients included in this study. Their help is gratefully acknowledged. It was possible to account for all the patients because of the enthusiasm and persistence of Miss Rebecca Tarshis, of the Department of Publications of The Portland Clinic.

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DISCUSSION

Millard S. Rosenblatt (Portland, Ore.): Dr. Nadal has reported an interesting series of cases. The controversy today is in regard to papillary carcinomas of the thyroid. Many of the members of this Association have discussed this subject. Dr. Duncan called our attention to the bizarre biological behavior of this group of tumors. He pointed out that their unpredictability has rendered evaluation of therapy most difficult. Our President, Dr. Stone, has agreed with him. Dr. Macdonald has proposed extracapsular total thyroidectomy with regional dissection of the thyroid area from internal jugular to internal jugular for papillary carcinoma. In the presence of proved unilateral lymph node metastasis, radical neck dissection is combined with the aforementioned procedure. Dr. Chester thinks routine radical neck dissection should be performed. Dr. McCorkle believes that total thyroidectomy is indicated in patients with operable carcinoma of the thyroid gland with certain exceptions, and he believes in surgical removal of the regional lymphatics. Dr. Howard has concluded that radical neck dissection with either hemithyroidectomy or total thyroidectomy is indicated. Dr. Baker concludes that the principles of surgery for cancer should be observed in these cases. Some of the other members of this Association who have discussed this subject are Drs. Clausen, Cohn, Dobson, Goldman, Norris, Pollock, Schlicke, Seabrook, Searls and Ward.

The cases recently reported from the Mayo Clinic by Bears and Wollner are worthy of consideration. They conclude that papillary carcinomas of the thyroid are an exception to the ordinary rules of surgery for cancer. A papillary carcinoma is a slow growing lesion, and if treated surgically when in an operable stage, the prognosis is excellent. The natural history of this disease and the excellent survival rates make these authors believe that papillary carcinomas do not always have to be treated by radical operation. The problems of myxedema and parathyroid tetany have to be considered in the more radical procedures. It seems unwise and unnecessary to extend an operation beyond the limits that will offer the patient a good chance of survival and cure. Papillary metastatic lesions spread by embolization and remain well encapsulated for long periods. Bears and Wollner do not perform standard radical neck dissection for papillary carcinoma unless the findings in each case indicate its necessity.

I would like to relate two cases from the Doernbecher Hospital. In 1948 a nodule was removed from the right side of the neck of a ten year old girl. After this was found to be papillary carcinoma the patient's family was advised that the child should undergo total thyroidectomy and right radical neck dissection. The family refused and the patient was taken elsewhere. Lobectomy was performed and at five different times malignant cervical glands were removed without a radical procedure being done. In 1958, ten years after the original carcinoma was discovered, she had no evidence of residual disease.

The second case is that of a fourteen year old girl who underwent right subtotal thyroidectomy for a nodule in her thyroid, which was identified as papillary carcinoma. Total right lobectomy and subtotal thyroidectomy were performed, along with radical neck dissection; the glands and thyroid were negative for disease. Although this patient has a satisfactory appearance compared to other cases of radical neck dissection, she has declined to attend school. She feels that her appearance is so conspicuous that she ostracizes herself from friends and even relatives.

The first patient, by our standards, has been inadequately treated and is still clinically well. The second patient has become a psychological invalid and recluse, at least for the time being, as a result of her radical surgery.

With the evidence described by Dr. Nadal and by the recent Mayo Clinic report, with considera-

tion for cases such as I have described, and despite some of the opinions quoted, one must still regard the planning of the surgical procedure for papillary cancer of the thyroid as a matter of clinical judgment.

GORDON S. FAHRNI (Vancouver, B. C.): Twenty-five years ago papillary carcinoma constituted 28 per cent of the malignant goiters in my practice. Since then, in a recent survey, the incidence of papillary carcinoma over follicular and other types has risen to 55 per cent. These figures are supported in a general way by other writers and clinics. Microscopic structural criteria demanded by different pathologists make an exact comparison quite difficult.

In discussing the treatment of this type of cancer of the thyroid, I would like to remind you that many papillary thyroid carcinomas grow slowly and are rather slowly invasive. Many of you, I am sure, recall the so-called aberrant thyroid nodule in the neck some twenty or more years ago which grew very slowly and after its removal was not considered malignant. We now know, of course, that these nodules were metastases to lymph nodes from a primary papillary growth in the thyroid lobe of the same side which remained dormant a long time.

When this was recognized about twenty years ago, I went through the records in the General Hospital of Winnipeg where I worked and found that some of the patients who had had aberrant thyroid nodules removed had no evidence of recurrence, while others who showed slow metastasis were cured again for indefinite periods of time after local removal.

This early experience has tended to steer me away from radical neck dissections when a malignant nodule of a papillary nature is found in one lobe. Up to a few years ago, I contented myself with performing simple total lobectomy with removal of the isthmus when no evidence of metastasis to lymph nodes was present.

About eight years ago I performed block dissection of the right side of the neck and complete removal of the right thyroid lobe together with the isthmus when a few metastatic nodes were found in the right side of the neck. Three years later this young woman returned with a nodule in the left thyroid lobe and metastatic nodes in the upper cervical area on the left side. Radical removal of the left lobe and block dissection of the left side of the neck has left her apparently well so far.

The lesson I learned from this case is that I should have performed total thyroidectomy at the original operation. It is presumed that the growth spread from the right to the left lobe but, of course, a second primary growth cannot be completely excluded.

In children thyroid nodules of a papillary character are not uncommon, and the solitary type seems more prone to be malignant.

For the record, I would like to make it clear that I believe when metastatic nodes of a papillary nature are present, block neck dissection should be carried out but when the disease is apparently confined to the thyroid, radical surgery of this gland should suffice for the present at least.

I believe that follow-up deep radiotherapy should be practiced. What I have said of papillary carcinoma of the thyroid does not apply to follicular nor to poorly differentiated types.

Many people endure the presence of a nodular goiter year after year with utter complacency, and not uncommonly this attitude is shared by their medical attendant. I would like to stress the significance of a long-standing goiter suddenly enlarging; this should be a danger signal. Over the years I have operated upon a number of these to find that the malignant changes were still confined within the capsule of the adenoma. On reviewing this group later, one is struck with the favorable prognosis that can be made if this danger signal sends them to surgery. To neglect it often means the arrival of a patient when anyone can make the diagnosis but nothing much can be done.

HENRY H. SEARLS (San Francisco, Calif.): In any discussion of cancer of the thyroid, there are a few rather definite angles in the problem from which one may safely project diagnosis and treatment. First, if a young patient has a tumor in the thyroid one may be reasonably certain that it is a true tumor and the percentage would indicate the balance in favor of a malignant tumor. Therefore, one should operate without delay, performing total lobectomy and isthmectomy on the side involved and request an immediate frozen section. In a very high percentage of instances the tumor will be either a benign adenoma or a papillary carcinoma. If the former, the operation may be considered completed and closure accomplished. If it is carcinomatous, most likely there has been spread to the opposite lobe and total thyroidectomy should be completed. Incidentally, it is my impression that any tumor of the thyroid, in any age group showing papillary architecture, is almost positively malignant, but usually has a very low grade of malignant characteristics.

WM. F. POLLOCK (Santa Monica, Calif.): In the January 1959 issue of *The Journal of Clinical Endocrinology* there is a paper from the University of California by Drs. Sheline, Lindsay and Bell on the appearance of thyroid nodules in three children following radioiodine therapy. One of these three nodules was a borderline malignancy.

I would like to bring to your attention the case of a child in whom the appearance of carcinona seemed unequivocally established after treatment of hyperthyroidism with radioactive iodine.

This twelve year old child was treated with radioactive iodine because she had a congenital heart disorder which was thought to prevent the possibility of surgery. In 1955 on the basis of a scintigram, uptake studies, protein-bound iodine values and other studies, it was concluded she had classic Graves' disease. There was no palpable nodularity of the thyroid gland. Everyone who saw this scintigram thought that the gland was enlarged with an increased uptake but that there was no evidence of nodularity. Her disease was treated with two courses of radioactive iodine.

About two years and three months later it became clinically apparent that a thyroid nodule was present. On scintigram it was apparent that there was a small area of decreased function here. At this time she was euthyroid by every test. She was operated upon for this nodule in January, 1958.

The diagnosis of papillary carcinoma has been confirmed by three independent pathologists.

I report this case because I believe there is a distinct hazard associated with the use of radioactive iodine in therapeutic amounts in children.

JOSEPH W. NADAL (closing): In carrying out our study and follow-up of these patients treated over twenty years ago, we had no particular thesis to try to prove or disprove. We were, however, able to find out what happened to all of them. If the treatment employed was inadequate in terms of present day concepts, then the results can at least serve as a sort of baseline with which to compare the results of more modern treatment.

In view of the high percentage of cures in the group of patients with papillary carcinoma, I have been asked why we are not ready to stop performing prophylactic neck dissections. Perhaps we should. However, I do not believe we should alter our present policy immediately merely on the basis of the results in this small series of cases. Of course, we do not now perform prophylactic neck dissections on every patient, as, for example, the patient with carcinoma in the thyroid isthmus.

The Present Status of Thymectomy in Myasthenia Gravis

A REVIEW OF THREE CASES

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THE present controversial feeling toward thymectomy and the value of its therapeutic effect on myasthenia gravis prompted us to review the current literature from abroad and from our own American clinics.

Two principal forms of attack on the thymus have been used, x-ray radiation and surgery. In 1921 Pierchalla [6] was the first to report improvement of myasthenia by radiation of the thymus. This form of treatment was soon abandoned.

In 1936 Blalock [2,3] removed a thymic tumor from a man with myasthenia gravis with concomitant improvement in the condition. Following this initial success, thymectomy has been performed upon small groups of patients, with appraisal of its merits, at the Massachusetts General Hospital, the Mayo Clinic and the Johns Hopkins Hospital, and by Keynes of London.

Keynes [5] is a most enthusiastic proponent of surgical therapy. The Mayo Clinic [4] has revealed a marked fluctuation in its enthusiasm for this form of treatment. They are now much more selective and believe that there is marked improvement in female patients with non-neoplastic thymus glands. The Massachusetts General Hospital [8,10] has recently concluded that one-third of patients were significantly improved with a few complete remissions and one-third were somewhat improved, while one-third showed no evidence of improvement.

The physiologic role of the thymus in normal and abnormal conditions such as myasthemia gravis has not been determined. A specific substance with a curare-like action has not been found. Wilson and Wilson [11] of Liverpool have produced a potent extract from thymic glands removed from patients with myasthenia gravis which in the laboratory produces the effect of nerve blocking ordinarily obtained with tubocurarine or decamethonium. This effect is not obtained from thymic glands of normal adults but is produced from infantile or fetal thymic tissue as well as from the fetal thymus of the whale. These thymic extracts do not produce the characteristic features of myasthenia gravis nor is the effect reversed by neostigmine.

The studies by Wilson and Wilson suggest that if the curare-like substance is released over a prolonged period of time, it may cause irreversible changes near or at the neuromuscular junction. These changes are not influenced by a late removal of the thymus although response to neostigmine is unaffected. Certainly this is a field which is wide open for basic research.

The following three patients with myasthenia gravis were treated by surgical removal of the thymus. The second patient had supplemental radiation therapy.

CASE REPORTS

CASE 1. J. G., a twenty-one year old white married woman with one child, was well until her senior year in high school.

She had felt well until the age of seventeen when she noted some difficulty in lifting her legs while walking upstairs and marked weakness in the thighs while dancing. Following graduation she was married and obtained a job as a file clerk. She noted increased difficulty in stooping over the files and increased weakness in her thighs. Following the birth of her first child her condition became rapidly and progressively worse. Progressive weakness developed in the arm and shoulder, and in six

months she was hospitalized. After a thorough study a definite diagnosis of myasthenia gravis was made. Improvement occurred after 1.5 mg. of intramuscular Prostigmin® was given. She was dismissed on a regimen of oral Prostigmin Bromide, 15 mg. every two to four hours. The myasthenia spread to other muscle groups and her requirements rapidly increased to 60 mg. every two to four hours. It was finally necessary to supplement the oral intake with intramuscular doses of Prostigmin Methylsulfate.

Clinical examination showed moderate bilateral ptosis, diplopia and typical myasthenic facies. The muscles of mastication and deglutition were so weak that eating was nearly impossible after two to three minutes. There was marked slurring of speech. Moderate dysarthria and all other classic symptoms of myasthenia developed. She frequently collapsed at home, many times being unable to dial the phone for help. Physical findings, aside from the general ones of myasthenia, were otherwise normal. Cystitis and slight leukopenia and anemia developed. The chest x-ray film was normal.

On January 25, 1955, the patient was operated upon through a sternum-splitting cervicothoracic incision. (Fig. 1.) The entire hyperplastic thymus was removed; it weighed 28 gm. Anesthesia included Pentothal,® nitrous oxide and oxygen.

The patient was awake immediately following surgery and was sent home on the eighth postoperative day. Her dosage of Prostigmin had dropped to 15 mg. every three to four hours orally at the time of discharge from the hospital. This dosage rapidly dropped to no Prostigmin or an occasional tablet when she worked hard. She became pregnant six months later and had no difficulty during or after pregnancy. She now works hard caring for her family and does outside work with no difficulty. She rarely takes Prostigmin. We consider this a near perfect result.

FIG. 1. Case 1. Operative specimen.

CASE II. T. C., a sixty-six year old white widow with two children, had been well until December, 1954, when she noted a feeling of heaviness in the back of her neck and shoulders followed by weakness. Slurring of speech and difficulty in swallowing developed. She was given physical therapy in the spring of 1955. On June 15, 1955, she reported to an internist because of marked diplopia which she had first noticed in April. She had lost about 25 pounds. She was recognized as having myasthenia gravis and was given Prostigmin, 7.5 mg. every four hours, plus 3 gr. of ephedrine three times a day. As she showed very little improvement after three months of treatment she started treating herself. She took oral Prostigmin in increasing amounts until she was up to 15 to 22.5 mg. every two hours, and eventually 15 mg. every hour. She had a cholinergic crisis on March 17, 1957, and was hospitalized. The dosage of Prostigmin was reduced and she improved.

Clinical examination revealed a pleasant, slightly wrinkled middle-aged woman in no acute distress. Positive findings included weakness of right lateral gaze, with diplopia. There was marked kyphosis of the dorsal spine. On auscultation a loud systolic murmur of mitral insufficiency was heard. Fluoroscopy of the chest revealed a heart of normal size. There was a large mediastinal mass just below the aortic knob. Her condition was fairly well controlled with Mytelase,® 25 mg. taken orally every three hours, but she was given, in addition, 15 mg. of Mestinon® orally every two hours during the day and every three hours at night.

Roentgenologic examination revealed an anterior mediastinal mass which appeared to be lobulated and encapsulated and was considered to be a thymoma.

On April 17, 1957, a large thymic tumor was removed through a cervicothoracic sternum-splitting incision. There was local invasion of the upper lobe of the left lung. Anesthesia included Pentothal, nitrous oxide, ether and oxygen.

The specimen was not weighed but measured 17 by 5 by 5 cm. The final diagnosis was thymoma within the nodular portion of the gland which measured 4 by 4 by 2 cm.

The patient's postoperative course was uneventful except for left pleural effusion. She went home on the tenth postoperative day. She has also received 4,000 r of radiation therapy* to the mediastinal area over a period of forty days. She continued to do well on a dosage of 7 to 8 Mestinon tablets daily and noted some improvement in general strength. She lives a quiet life at home, does much painting and is ambulatory. Fluoroscopy of the chest shows a normal heart and no mediastinal mass.

Comment: We believe that in this case thymectomy was definitely lifesaving. The patient undoubtedly would have died of the thymic tumor without surgery as her myasthenia was getting progressively worse. It has remained stationary ever since with some improvement.

CASE III. J. H., a twenty-four year old white married woman, para 1, gravida 11, was first seen on October 10, 1957, complaining of myasthenia gravis of two years' duration.

In 1955 she had noted progressive weakness of all muscle groups which was most marked on walking and holding up her arms. She went to several doctors and finally in October, 1955, a diagnosis of myasthenia gravis was made and she was given Prostigmin. She continued on this regimen until June, 1956, when she was taking 50 mg. every five hours. In July, 1956, after having become pregnant in June, she had a therapeutic abortion because of serious illness and severe respiratory distress which necessitated her being placed in a mechanical respirator. After this she was given Mytelase, 200 mg. daily in divided doses of 40 mg. every four hours. After about three hours this drug was relatively ineffective and she became very weak. Her course continued downhill, and at the time of hospitalization she was confined to bed most of the time.

Clinical examination revealed a small, very weak, well developed young woman in no acute distress. Her skin was sallow and warm. Her upper lids drooped markedly and her head would fall forward on her chest until she was given Prostigmin. She swallowed rather poorly. There was marked slurring of speech. The extremities were very weak and repetitive actions such as knee-crossing and squatting were completely impossible. In fact, she was unable to hold her hands up for more than about twenty seconds. Even after a fresh dose of Prostigmin she was unable to hold up her arms for more than sixty seconds. She walked with a waddle, with the feet spread apart. Walking became impossible after more than five minutes. X-ray examination of the mediastinum was negative for abnormalities. The heart was normal in size and configuration. The patient was given two 60 mg. Mestinon tablets every three hours. During the next month she was seen frequently in her home and given injections of Prostigmin Methylsulfate as she was so weak she could not swallow pills. Finally a regimen consisting of 60 mg. of Mestinon at nine, one and five o'clock and 50 mg. of Mytelase at seven, eleven, three, seven and ten was instituted. She progressed fairly well on this for awhile until about December, 1957, when she began to go downhill very rapidly. Because of her progressive downhill course it was decided to perform surgery.

On December 27, 1957, the patient was operated upon through a sternum-splitting cervicothoracic incision. Anesthesia included Pentothal-nitrous oxide-oxygen.

Pathologic examination showed that the thymus gland weighed 13 gm. and measured 15 by 2 by 4 cm. The final diagnosis was medullary lymphocytic hyperplasia.

Postoperatively a marked therapeutic rebound developed and she felt so much better she was able to cut her Mytelase dosage down to about 30 mg. She could do five leg-crossing tests which was the most she had ever done, and straight-arm extension lasted over a minute. By April, 1958, she had reduced her medication of Mytelase to 15 mg. in the morning and 20 mg. every four hours. However, she began to note increasing weakness again at this time. On her last visit, October 16, 1958, she was nearly as incapacitated as when first seen. She was taking 25 mg. of Mytelase every four hours and 50 mg. of Mestinon every two hours.

Comment: We believe that thymectomy in this case arrested the downhill course temporarily and perhaps prolonged the patient's life by several years. The effects of stress [1,9] produced by surgery must also be considered in the evaluation of marked but temporary postoperative improvement.

THERAPEUTIC REGIMEN

Preoperative preparation of the patient should include adequate adjustment of Prostigmin instead of Mytelase or Mestinon. All signs of infection should be controlled. Prophylactic antibiotic therapy is practiced. Female patients should be operated upon in the postmenstrual period. Premedication includes 0.5 to 1.5 mg. of Prostigmin Methylsulfate, 10 mg. of morphine sulfate and 0.4 mg. of atropine sulfate given subcutaneously. Viets [8] has calculated the intravenous dose of Prostigmin to be one-thirtieth the oral dose. We have included one-third of the

*At the Tumor Institute, Swedish Hospital, Seattle.

total daily dose in 1,000 cc. of 5 per cent glucose in distilled water as the intravenous dose to be given over eight hours during and following surgery.

During operation the anesthesia of choice is cyclopropane or Pentothal with nitrous oxide-oxygen mixture. Long-acting barbiturates and curare are obviously to be avoided. The operative procedure is begun with a "T" incision (Fig. 2), splitting the sternum to the fourth or fifth interspace. This is readily accomplished with the Lebsche sternum chisel. A limited use of bone wax has controlled sternal bleeding. A very careful dissection of the entire gland including the cervical extensions is essential to its complete removal. Closure of the sternum has been accomplished with multiple periosteal sutures of multifilament nylon (Zytor®) or wire. A temporary suprasternal drain has been of value.

Postoperatively special nurses should care for these patients around the clock. These nurses should be trained in the recognition of myasthenic symptoms and cholinergic crisis. Adequate oxygen should be given, a respirator should be on hand and a tracheotomy set should be immediately available. The dosage of Prostigmin and atropine is dictated by the individual case. Intravenous infusions should be kept low the first twenty-four hours, at less than 2,000 cc. Other care is similar to that after any thoracic operation.

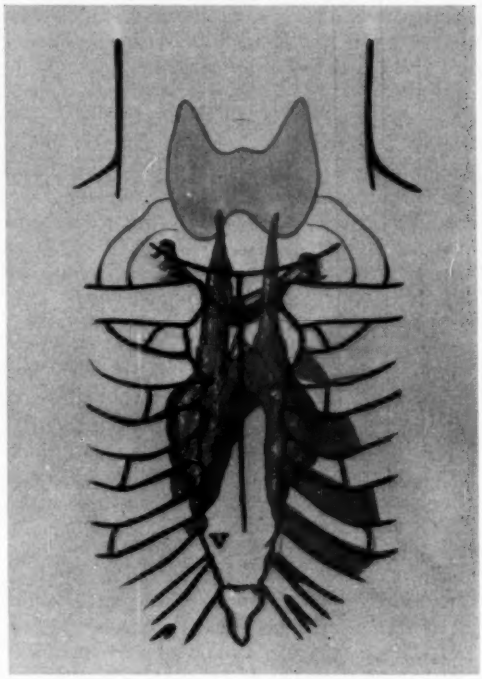

FIG. 2. Sketch of anatomic relations with superimposed lines of "T" skin incision over the sternum. The sternum is split down to about the fifth condrosternal junction, as marked by "v."

COMMENTS

Earlier reports on the results of thymectomy were controversial due to two facts: (1) evaluation of a disease with spontaneous remissions is difficult, and (2) in the earlier series all cases of myasthenia were lumped together and no adequate controls were available. Some results seemed to indicate that all patients should undergo thymectomy and others suggested that it be abandoned altogether.

Later reports from the larger centers have been based on series in which cases and controls have been classified according to age, sex, duration of symptoms and presence or absence of thymoma. Gradually a set of fairly well established indications has developed.

Most investigators agree that women without thymomas should be operated upon, especially if they are young and the disease is of short duration. In the series from Massachusetts General Hospital and the Mayo Clinic, women who underwent thymectomy had complete remissions or marked improvement twice as often as women in the control group.

General agreement also exists that the shorter the duration of symptoms, the better the prognosis. The fact that more cures occur in the younger group, however, may be weighed by the fact that female patients under forty outnumber males, whereas over forty the reverse is true, as shown by the Mayo Clinic figures. In no series are there sufficient statistics to evaluate women over forty properly.

All groups report disappointing results in males. This varies from statistically little or no improvement at the Mayo Clinic to the even poorer results of Schwab and Leland [7] whose control series did better than those who underwent exploration. These authors believe that operation is contraindicated in males over thirty, while the Mayo Clinic considers each case individually.

More statistics are needed concerning thymectomy in cases of thymoma. These patients

usually are older, have more severe myasthenia, are a higher operative risk and have a relatively poor postoperative prognosis. None of the centers have enough cases to break down into groups. The Mayo Clinic believes that operation may be of value in females, while Keynes suggests that preoperative radiation might improve results. In addition, one must consider the operability of the tumor itself and the risk of extension locally. Until better statistics are available, these cases must be considered on their individual merits.

SUMMARY

A short review of the current literature has been made. The three cases presented of myasthenia gravis treated by thymectomy tend to support the conclusions drawn by larger groups with a statistically significant series of cases. The preoperative, operative and postoperative care has been outlined.

CONCLUSIONS

1. Most young women with myasthenia gravis of two to three years' duration and no evidence of thymic tumor should undergo exploration.

2. Thymectomy is of doubtful value after ten years' duration of symptoms.

3. All patients with suspected thymic tumors without myasthenia gravis should undergo exploration, as well as those with concomitant myasthenia gravis, but only after careful evaluation. One should carefully balance the risk against the possible benefits.

4. Thymectomy in male patients has not been completely evaluated but is considered to be of doubtful value.

5. Radiation therapy is of questionable value but is used in patients who are poor operative risks.

6. Further studies on the basic pathologic physiology of this disease is essential to its successful treatment.

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DISCUSSION

William P. Longmire, Jr. (Los Angeles, Calif.): First, may I compliment the authors on their review of the current concepts of the etiology and therapy of this fascinating, puzzling disease and for their comments on the operative management of their cases.

Due to the interest of Dr. Augustus S. Rose and his colleagues in the Neurological Clinic, seventy-eight patients with myasthenia gravis have been seen at the U.C.L.A. Medical Center since July 1954. During the three and a half years the U.C.L.A. Hospital has been open, eighteen patients were admitted for evaluation or treatment; they served as the basis for the following survey. There were fourteen female and four male patients. The age distribution at the time of onset of the disease was as follows: neonatal, two; one to ten years of age, one; eleven to twenty, five; twenty-one to thirty, three; thirty-one to forty, one; forty-one to fifty, three; fifty-one to sixty, two; and over sixty, one.

The neonatal cases were both female infants born to mothers with myasthenia gravis. Signs of muscular weakness became apparent on the second day postpartum as evidenced by a poor sucking and coughing reflex, and excessive salivation. The babies were treated by intermittent oropharyngeal suction, gavage and Mestinon, 5 mg. four times a day. In both babies the symptoms were transient and medication was discontinued by the fourth week postpartum. One of the patients in this series, a mother with myasthenia gravis, was admitted immediately following parturition at another hospital. Her female infant was also reported to have had mild transient symptoms of myasthenia gravis.

It is generally considered that in approximately one-third of the infants born to mothers with myasthenia gravis such symptoms will develop. The transient nature of these symptoms is assured.

Major associated diseases developed in five patients during the course of myasthenia. In two, thyrotoxicosis developed with exacerbation of myasthenic symptoms. These symptoms improved following treatment of the thyroid condition. Adenocarcinoma of the uterus, grand mal epilepsy and acute rheumatoid arthritis each occurred in separate patients.

Cobalt radiation to the thymus was employed in the treatment of four patients. Two have shown improvement for over one year. No improvement was noted in the other two patients.

Three patients have been treated by thymectomy. Improvement was maintained by one patient operated upon elsewhere for approximately ten years until the onset of thyrotoxicosis. The other two patients have also shown improvement. One was a six and a half year old girl with severe progressive myasthenia whose symptoms have been greatly relieved for one year, the other a nineteen year old girl whose condition was considered improved for four months following operation.

Two patients in this series have died during the course of medical treatment. A malignant thymoma with widespread metastasis was found at autopsy in one patient. The other died of uncontrollable generalized weakness, pneumonia and cardiac failure. One additional patient, who was discharged in a respirator in chronic condition, has not been traced but is probably dead. There have been no deaths in the patients undergoing thymectomy.

The relationship of the thymus gland to this disease is not understood, and the selection of patients for thymectomy is, therefore, an uncertain process. In general, female patients under the age of twenty-eight with myasthenia of short duration (less than two years) and without evidence of thymoma are considered to be in the group who may most consistently be benefited by thymectomy.

Again, I wish to compliment the authors for their timely presentation of a most interesting condition which may occasionally be benefited by surgical removal of the thymus gland.

HILDING H. OLSON (closing): As mentioned in our paper, the patient in Case II, an older woman with a thymoma, received radiation therapy at the Tumor Institute at Swedish Hospital. A total of 4,000 r was given over a forty-day period. It is their opinion that radiation therapy should be given very slowly in the beginning since they have had one death when it was given too fast and in too large a dosage.

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Current Concepts of Thymomas

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THERE has been, in the past, considerable difference of opinion concerning the pathological and clinical characteristics of thymic tumors. This stemmed partly from the lack of a precise definition of what constituted a tumor of the thymus gland. Most of this confusion disappears if a thymoma is defined as a tumor arising from the parenchyma of the thymus gland containing epithelial (reticulum) cells and thymocytes (synonymous with lymphocytes) [*4,25*]. These tumors are grayish white to pinkish orange in color, lobulated, and usually encapsulated. Microscopically they may show varying degrees of cystic change, necrosis, calcification, fibrous stroma, and abortive Hassall's corpuscles. However, they all contain the two basic cell types (reticulum cells and lymphocytes) in varying proportions or they cannot properly be called thymomas. This eliminates from discussion other anterior mediastinal tumors including teratomas, enteric and dermoid cysts, germinomas [*29*], benign hyperplasia of mediastinal lymph nodes, involvement of lymph nodes by malignant lymphomas (including Hodgkin's disease) and small cell bronchogenic carcinoma. (Fig. 1.)

Peculiar to thymomas is their lack of embolic metastases either by way of the blood or lymph streams [*4,25*]. Much like basal cell epitheliomas of the skin their malignant nature is manifested by direct invasion and implantation. In thymomas this spread is to the pleura and vital mediastinal structures. McBurney et al. [*19*] described a case of a primary intrapulmonary neoplasm associated with myasthenia gravis in which there was no mediastinal tumor. They believed this to be an ectopic thymoma. Derow and co-workers [*6*] recorded a case of myasthenia gravis with an invasive thymoma in the mediastinum and a solitary secondary intrapulmonary thymoma. This could presumably have been an embolic metastasis but most likely was secondary to necrotic erosion of the mediastinal thymoma into a large bronchus with consequent bronchogenic spread. Morgan and Dudley [*20*] described a patient with an inoperable thymoma of over ten years' duration with spread of the tumor throughout the mediastinum, into the neck and through the diaphragm retroperitoneally. There was also a solitary nodule in the right lobe of the liver found at necropsy which could have entered the blood stream at the time of a previous surgical exploration or could represent a true blood-borne metastasis. Effler and McCormack [*8*] recorded a case of metastasis to the submaxillary gland probably via the lymph stream. Nevertheless, if embolic metastases do occur they do so rarely, and are not to be considered characteristic.

Likewise, thymomas display few histologic features of malignancy [*4,25*] such as hyperchromasia, increased nuclear-cytoplasmic ratio, and mitotic figures. This is true even of thymomas which are not resectable because of gross invasion of contiguous structures. Therefore, it is the surgeon and not the pathologist who determines whether the tumor is benign or malignant in these interesting cases. (Fig. 1.)

Finally, thymolipomas are not to be confused with thymomas. Thymolipomas are merely lipomas which originate from fat cells normally found in the thymus gland, and behave in the same manner as lipomas elsewhere in the body.

Thymomas are practically always found to lie in the anterior mediastinum, occur in both male and female, and in children and older people. They are usually asymptomatic until they encroach on neighboring structures when pain, dyspnea, and signs of superior vena caval obstruction may appear. However, non-resectable malignant thymomas may be entirely

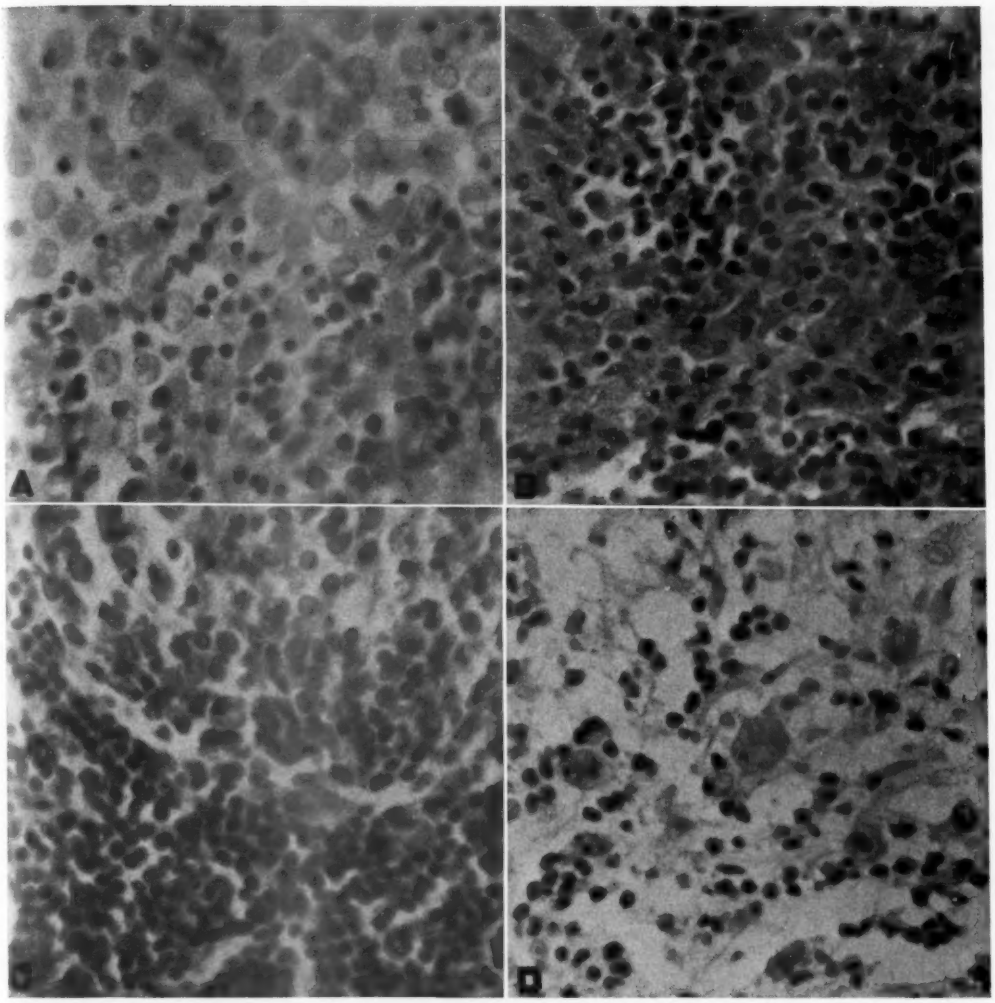

FIG. 1. A benign thymoma associated with myasthenia gravis, note epithelial cells and lymphocytes. B, similar histologic picture of another thymoma which invaded mediastinal structures. Note absence of histological characteristics of malignancy. C, benign hyperplastic mediastinal lymph node simulating thymoma. Upper portion of section is a germinal center. D, Hodgkin's disease. Reed-Sternberg cells and eosinophilia distinguish this from thymomas.

asymptomatic and remain so for a long period of time [*20*]. Uusually the presumptive diagnosis is based upon finding an anterior mediastinal tumor near the aortic arch and base of the heart on a routine chest film. However, the smaller thymomas can be missed on the posteroanterior roentgenograms. Therefore, if a tumor is suspected, as it is in any case of myasthenia gravis, it is necessary to use the fluoroscope, to take lateral and oblique films [*25*], and possibly to perform lateral tomography [*13*] to disclose the lesion. (Fig. 2.)

No discussion of thymomas would be complete without considering their relationship to myasthenia gravis. In 1901, Weigert [*27*] first described a case of myasthenia gravis associated with a thymic tumor. After more than half a century our knowledge of this mysterious inter-relationship has progressed little. Interest in the problem was rekindled in 1936 when

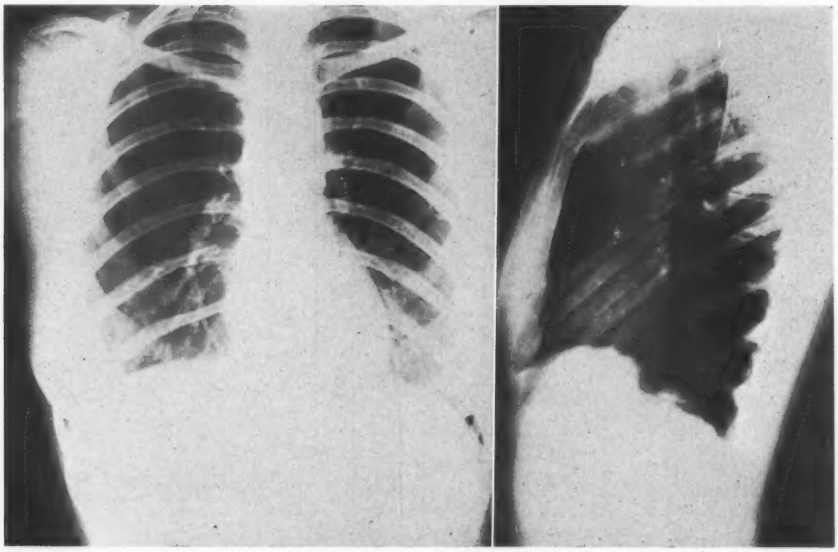

FIG. 2. Posteroanterior view of chest is normal. However, large anterior mediastinal tumor is seen on lateral film. This proved to be a thymoma in a myasthenic patient.

Blalock [3] successfully removed a thymic tumor in a myasthenic patient. Previously this had been attempted unsuccessfully by Sauerbruch who met with failure because of deaths caused by infection during the postoperative period. Blalock's patient experienced a clinical remission of the disease, and this stimulated the subsequent removal of many apparently normal thymus glands as well as thymomas in the hope of effecting remissions or cures.

Approximately 15 per cent of patients with myasthenia gravis have thymomas [7,13]. As more indeterminate mediastinal lesions are being explored, more thymomas (now probably 50 per cent) are being discovered which are not associated with myasthenia. However, an anterior mediastinal tumor in a myasthenic patient is almost certain to be a thymoma.

There seems to be no definite histologic pattern by which one can distinguish a thymoma in a myasthenic patient from a thymoma in one who is free of the disease. However, Castleman [4] believes that the epithelial cells, which are spindle-shaped, are indicative of exhausted non-functioning cells and are, therefore, not seen in myasthenic patients. Nevertheless, his diagnosis was accurate in only 75 per cent of cases using this criterion as a basis for differentiation. It has been definitely established, that the benignancy or malignancy of thymic tumors has no relationship to the presence or absence of myasthenia gravis [20]. Furthermore, thymomas can occur either before or after the appearance of myasthenia, and there are cases in which myasthenia has developed during the early postoperative period following the removal of a thymoma [9,11].

The great difficulty in assessing the results of any treatment for myasthenia gravis is the spontaneous remissions and exacerbations which typify the untreated cases. However, the number of long term remissions among the untreated or medically treated cases, is not as great as it is following thymectomy [16,23]. Of interest is the fact that when myasthenia gravis is associated with a thymoma the results of surgical removal of the tumor are, in general, less likely to be successful than with a non-tumor bearing thymus [24]. Keynes [17] goes so far as to exclude thymomas from his series as he believes they are associated with a particularly virulent type of myasthenia. In his opinion Eaton et al. [7] obtained few striking remissions as a result of surgery because they did not exclude thymomas from their original studies. However, remissions do occur following the removal of thymomas in a certain percentage of cases. (Fig. 3.) Whether or not to

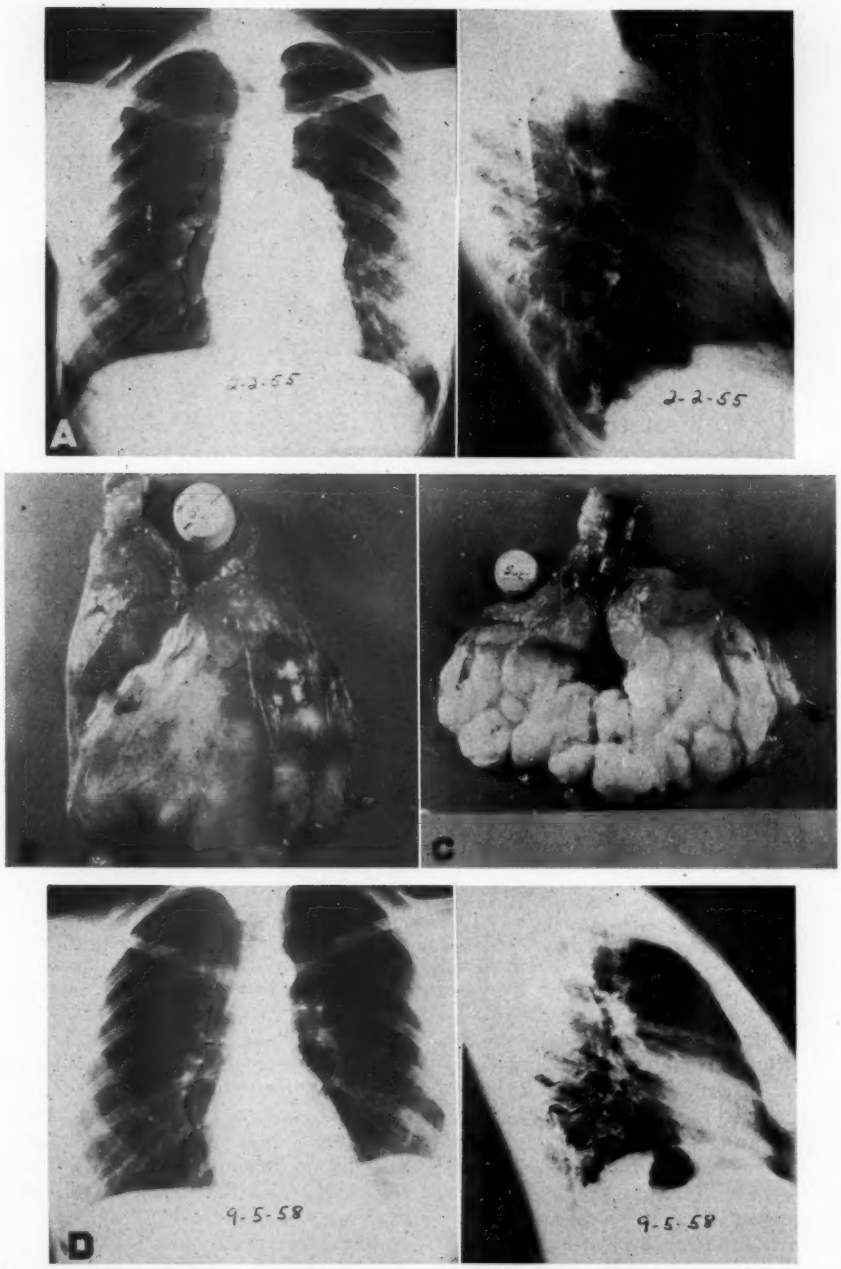

FIG. 3. A, posteroanterior chest films of thirty-three year old woman with severe myasthenia gravis of short duration. B, gross specimen of resected thymoma. Note the H-shaped appearance. C, same specimen showing cut surface and typical lobulation and encapsulation of benign thymomas. D, chest film taken three years postoperatively. To date patient has experienced a complete remission of her disease.

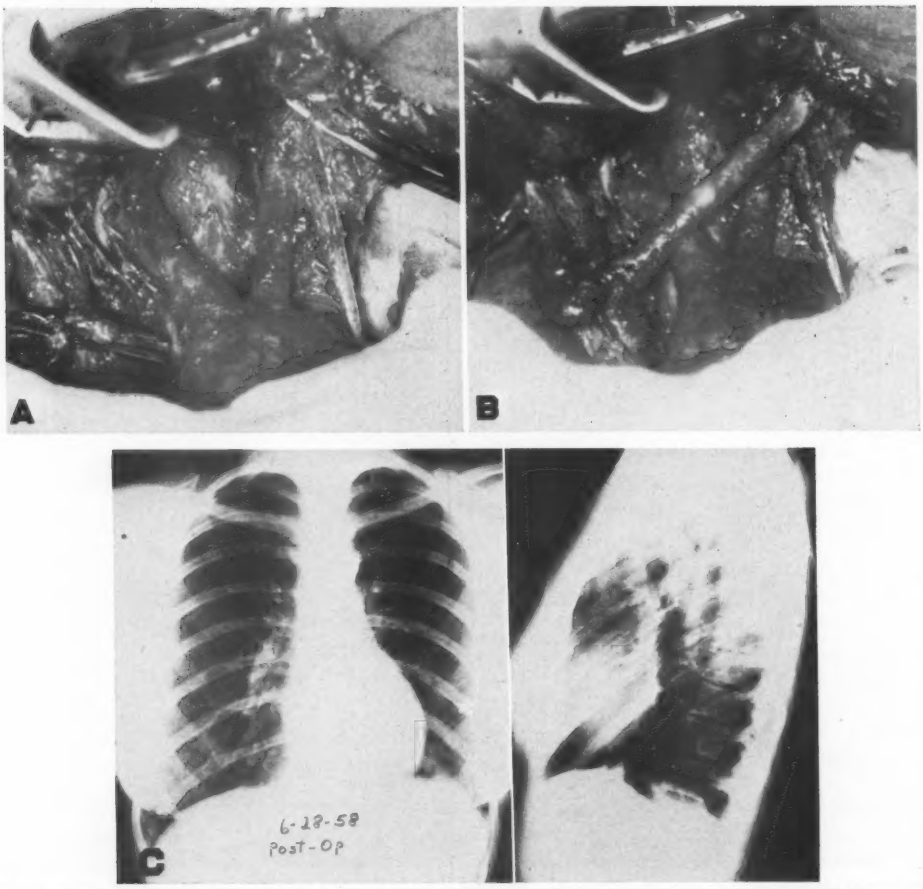

FIG. 4. A, upper mediastinal dissection through trans-sternal incision of invasive thymoma in a young girl with myasthenia gravis. Note aortic arch, great vessels and left vagus nerve. The left innominate vein and left phrenic nerve were removed with the tumor. Note Potts' clamps on proximal and distal ends of the left innominate vein which is ready for anastomosis. B, anastomosis completed with arterial homograft (iliac artery). C, Roentgenographic appearance of chest postoperatively. Patient is alive and living normally two and a half years later. She is still taking small doses of Mestinon.®

remove the thymus gland when there is no tumor present in a patient with myasthenia gravis is determined by the age and sex of the patient and by the severity and duration of the disease. The best results seem to be obtained in young females who have the shortest history and the more severe form of the disease [*16,23*]. In about two-thirds of such patients improvement should follow thymectomy.

Recently still another seemingly unrelated disease has been associated with the presence of a thymoma. In patients with severe refractory anemias, mediastinal tumors characteristic of thymoma have been reported [*5*], although we have not personally encountered them. Removal of the tumor has been of benefit in four of eleven cases [*5,14*], but in the majority there was no improvement in the hematopoietic response [*1,22*]. Unfortunately, when this is true, any other therapy, such as steroids, splenectomy or blood transfusions is only palliative. One case [*28*] was associated with myasthenia gravis to make the condition even more intriguing, while another [*15*] caused depression of the white cell precursors in the bone marrow as well as of the red cells leading

to a pancytopenia. Since most of the thymomas were present before the development of anemia, and the anemia was cured in some patients by the removal of the tumor, some specific relationship is implied.

Agammaglobulinemia has also been found in association with thymomas. In three cases reported in the literature [*12,18,21*] there was, in addition to the agammaglobulinemia and thymoma, some blood deficiency; a lack of eosinophils in one, and severe anemia in the other two. The number of cases of agammaglobulinemia might well be larger, had all the cases of aregenerative anemia been studied in regard to the blood proteins. The exact common denominator, however, linking thymic tumors, myasthenia gravis, aplastic anemias and agammaglobulinemia remains annoyingly elusive.

Because of their malignant potential (10 to 25 per cent) [*4,25*] we believe that all thymic tumors should be explored and resected if at all possible, regardless of whether or not the patient has myasthenia gravis. Every effort to eradicate the tumor surgically must be made because in the absence of embolic phenomena even invasive types may be cured. Resection and grafting of the great vessels may be required to completely remove the tumor. This has been performed successfully in one of our cases by substituting an arterial homograft for the left innominate vein. (Fig. 4.)

Thymomas may best be approached surgically through either a standard posterolateral thoracotomy incision or by splitting the sterum, depending on the size and location of the tumor. We prefer the former incision for the removal of any large tumor easily seen on a posteroanterior chest film, while the latter incision affords excellent exposure for the removal of the smaller ones which are usually visualized only by specialized views in patients with myasthenia gravis. It is the patients with myasthenia gravis who are poor operative risks, and for them the postoperative period can be a hazardous one. Prostigmine methyl sulfate is given in ample doses intramuscularly, and at the slightest sign of respiratory distress the patient is placed in a respirator which has been held in readiness in the room.

Difference of opinion exists concerning the effects of roentgen therapy in the treatment of thymomas, although all are agreed that it should never be used in lieu of surgery. Keynes' [*17*] results following the removal of thymomas in myasthenic patients were poor so that he advocates preoperative and often postoperative radiation. Others give postoperative roentgen therapy routinely following the removal of all thymomas [*8,10*]. We and others [*2,25*] would use radiation in only those cases in which the tumor could not be completely resected. The beneficial effect of ACTH therapy on ineradicable thymic masses has also been reported [*26*] but we have had no experience with this.

SUMMARY

In the past confusion has reigned concerning the treatment, prognosis and malignant potentialities of thymic tumors. This occurred mainly because there was no uniformity of opinion concerning the microscopic characteristics of the tumor. If we consider thymomas to be tumors which are composed always of two cell types, namely, the epithelial cell and the classic thymocyte (lymphocyte), they fall into a very definite pathologic and clinical entity. Thus they can be distinguished readily on both these grounds from other small cell tumors of the mediastinum, such as lymphoma, oat cell bronchogenic carcinoma, teratoma or germinoma.

These tumors rarely show embolic metastases but are potentially malignant by virtue of their capacity to invade vital mediastinal structures. Even when they do so the usual histologic criteria for malignancy are lacking. Therefore, it is essential that surgery be radical, perhaps necessitating the excision and grafting of involved great vessels, as surgical extirpation is the only method of cure. Roentgen therapy is palliative only but should be used in inoperable cases.

The association of thymomas, myasthenia gravis, agenesis of erythrocytes, and agammaglobulinemia remains an interesting and puzzling problem. That inter-relationships exist between these entities seems irrefutable, but the exact mechanisms involved remain tantalizingly obscure.

In conclusion we believe that all thymomas, whether associated with myasthenia or not, should be removed because of their malignant capabilities. Whether or not to remove the thymus gland from patients with myasthenia gravis depends upon the sex and age of the patient and the severity and duration of the disease.

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DISCUSSION

David J. Dugan (Oakland, Calif.): The roentgenographic appearance of an abnormal shadow in the anterior mediastinum is a well admitted indication for surgical exploration as has been so well emphasized by Drs. Jamplis and Cressman. While the majority of these undiagnosed lesions prove to be benign and are easily removed from the surgeon's and more certainly from the patient's point of view, thymic tumors are by far the most important. Complete and radical excision of the tumor together with visible local metastases offers the best chance of cure regardless of the histology of the thymoma.

Dr. Paul Samson and I have had occasion to treat nine patients similar to those under discussion today and the results to date tend to agree with the convictions of the authors. In all nine cases, with the exception of one, roentgenographic studies showed asymptomatic lesions of the anterior mediastinum. In the one exception there were signs of superior vena caval obstruction, and the case was completely inoperable. Five of the nine patients had non-resectable local metastases, and all were treated postoperatively with radiation; they died within six months of the diagnostic

thoracotomy. Of the remaining four patients three had well encapsulated lesions which showed no indication of extension. All three are alive and well five to seven years following surgery. The remaining patient would seem to warrant emphasis. This forty-five year old woman was first seen by us in 1948. Roentgenographic study showed a small anterior mediastinal nodule best seen on a slightly oblique film. At operation a lemon-sized tumor of the thymus, microscopically consistent with those described today, was resected. During the same operation several pleural implants presenting one identical histologic pattern were removed. Because of the implants the patient was treated postoperatively with radiation. She remained asymptomatic for nine years, then roentgenograms disclosed evidence of pleural metastasis and there were clinical signs of superior vena caval obstruction. Radiation therapy was repeated and her symptoms and signs disappeared. The patient is alive today. However, last week (ten years after mediastinotomy) we saw her again and there are signs of mediastinal recurrence of tumor.

This experience, together with that of others in the field, merely emphasizes the need for prompt surgical excision of all undiagnosed mediastinal lesions.

Ralph D. Cressman (Palo Alto, Calif.): There are two more conditions which have been associated with tumors of the thymus: refractory anemia and agammaglobulinemia.

Up to 1958, sixteen cases of refractory anemia associated with thymomas were reported. In two of these cases, the patients also had myasthenia gravis. The relationship of suppression of erythrogenesis and thymic tumor is considered by Bayrd and Bernatz to be proved by the response to excision of the thymoma. However, the nature of the relationship is obscure. The clinical picture is that of profound refractory anemia unless myasthenia is also present. The spleen may be enlarged (three cases) but is usually not palpable. Purpura has been present (two cases); the reticulocytes are reduced or absent. The leukocytes and platelets are usually normal, but granulocytopenia was present in three cases and thrombocytopenia in four. The bone marrow consistently shows depressed erythrogenesis.

Therapy has consisted of thymectomy in eleven patients resulting in two remissions, two partially improved after splenectomy and the administration of steriods, and seven with no improvement. In this last group of patients no therapy was beneficial.

William B. Hutchinson (Seattle Wash.): I would like to discuss three patients who were operated upon thirteen, twelve and ten years ago, with thymomas that have not recurred. The preoperative diagnosis was missed in each instance as the diagnosis was dermoids. As Dr. Jamplis mentioned, most thymomas are asymptomatic and often discovered inadvertently.

I would like to point out, the encapsulation of these thymomas, the hemorrhagic areas, the granular cut surface and the lobulation noted where the septum comes down and separates these tumors into lobules.

Follow-up is important in these patients because there is a good possibility that myasthenia gravis will develop in some of them at least, and it behooves us to follow them for long periods.

In the second case that Dr. Alson discussed I thought it was of interest to see how far superiorly the tumor went into the neck.

In Dr. Jamplis' case, in which resection was so extensive, the tumor also went into the neck. This emphasizes the importance of remembering that these tumors develop in the third pharyngeal pouch, and descend so that they actually may be found in the lower part of the neck, in the mediastinum, or even as far down as the diaphragm, as a few have been reported.

One other point, about blood-borne metastases. There are many eminent authorities in the field of pathology who believe that this simply does not exist and that if these patients are carefully studied and explored for direct extension this can be uncovered.

H. Brodie Stephens (San Francisco, Calif.): I would take issue with Dr. Jamplis on his statements regarding radiation.

One cannot be too careful in the utilization of this agent, and if one believes that one has removed all the tumor, then I think by all means radiation should not be used.

Under my care at the present time is a woman who has been suffering from the ill effects of deep radiation therapy for many years. There has been no recognizable evidence of recurrence of the malignant thymoma that this patient originally harbored. The patient suffers from a harrassing cough and repeated bouts of pulmonary bleeding originating in a fibriotic and bronchiectatic lung. It is my belief that these changes in the lung were brought about by radiation therapy. As a result of this experience I employ radiation in the treatment of malignant thymic tumors only when the tumor is inoperable.

I would appreciate learning from Dr. Jamplis when he decides that the thymoma has become persistent and surgical removal is recommended? In other words, does Dr. Jamplis believe that every persistent thymus should be excised, and at what age does he consider that the thymus has become persistent?

Lyman A. Brewer, III (Los Angeles, Calif.): We have been interested in the problems involved in the management of mediastinal tumors for a number of years. In a series of 165 operations for

neoplasms of the mediastinum, thymoma was found to be the third most common tumor. The neoplasms of neurogenic origin comprise 25 per cent of the cases, teratoid 18 per cent and thymomas 8 per cent. The thymomas occurred with the same frequency as did pericardial and bronchial cysts. Thus, we are concerned with an important mediastinal tumor, one which is being discovered more and more on routine roentgenographic surveys.

Recently we reviewed a series of twenty-nine patients; thirteen of our own operative cases and sixteen from the California Tumor Registry at the Los Angeles County General Hospital. One-third of these cases were completely asymptomatic and were discovered on routine x-ray films of the chest. Fifty-six per cent of these new growths proved to be malignant. It is quite interesting that routine postmortem studies show a low incidence of completely benign thymomas, so the inference is that the majority of these tumors eventually become malignant.

Thus there can be no doubt that it is vitally important to remove tumors of this group because they are potentially malignant, and because their size and location jeopardize the vital organs of the mediastinum. If treated surgically when they are localized and comparatively small, complete cure can be anticipated. In localizing these shadows of the mediastinum, the lateral planogram has been helpful to us in evaluating their exact position. Of course, the exploratory thoracotomy gives a more accurate picture of the situation, yet the determination of whether or not operation is necessary can be made by a careful roentgenographic study, including planograms and endoscopy; occasionally angiograms will be found necessary. Once the surgeon has opened the chest he is actually in a better position to determine whether or not any given tumor is benign or malignant than the pathologist. This seems a paradox, yet in the case of thymomas it is true. It is difficult for the pathologist to tell from the microscopic section whether you are dealing with a malignant lymphoma or thymoma. A surgeon can tell whether there is localized invasion or not. However, in either case the best treatment is to remove the tumor completely and if a thymoma or lymphoma is found as a result of careful paraffin section, then deep radiation therapy should be employed as a follow-up treatment. We have a number of long time survivals in asymptomatic patients who apparently have been cured by the combination of surgery and postoperative radiation therapy. On the other hand, deep x-ray therapy should not be given indiscriminately for any mass in the mediastinum. For a number of years, we have been very strict in demanding cellular diagnosis for this type of lesion. Needle biopsy of the mediastinum is very dangerous and should be confined to obviously inoperable cases in which the tumor mass is very close to the chest wall. Thus in the great majority of cases it will be necessary to perform a thoracotomy in order to establish the diagnosis. This is a safe procedure, as shown by the fact that we have had no mortality in our series of 165 cases that were directly referable to the thoracotomy.

When exploring the anterior mediastinum for a supposed mediastinal tumor, the surgeon must caution the anesthesiologist concerning the use of the curare-type of drugs. Occasionally in cases of thymoma there is a latent or minor degree of myasthenia gravis present. The use of these curare drugs may result in respiratory or skeletal paralysis which may well mitigate the success of the operation. Thus, in exploring an undiagnosed anterior mediastinal tumor in particular, these types of drugs are to be avoided. Certainly we have come a long way since the days of Galen who regarded the thymus as a pad to protect the vital organs of the mediastinum from the rough and rigid sternum.

ROBERT W. JAMPLIS (closing): To answer Dr. Stephens' question "at what age would we remove a thymoma?" I would say that any child over three or four years of age who has a visible mediastinal tumor should be explored, particularly if there are no x-ray films going back to infancy. We have performed an exploratory on a child six years old in whom we expected to find a dermoid or teratoid, instead we found a large encapsulated thymoma.

Again, we believe that radiation therapy should be confined to those tumors which cannot be completely eradicated surgically. However, we would have no quarrel whatsoever if radiation therapy was employed either because the surgeon did not believe he had removed the tumor completely or because the case was completely inoperable.

A New Method for Measurement of Lymph Flow from the Right Duct in the Dog

SANFORD E. LEEDS, M.D., HERMAN N. UHLEY, M.D., JOHN J. SAMPSON, M.D. AND MEYER FRIEDMAN, M.D., WITH THE TECHNICAL ASSISTANCE OF ELEANOR F. BAIRD, A.B. AND SHANTILAL PATEL, B.S., *San Francisco, California*

From the Harold Brunn Institute, Mount Zion Hospital and Medical Center, San Francisco 15, California. Aided by grants from the United States Public Health Service and the San Francisco Tuberculosis Association.

SINCE Warren and Drinker in 1942 developed a method of measuring lymph flow from the right lymphatic duct, considerable information has been acquired regarding the lymph flow from the lungs and its relation to pulmonary edema and inflammation. Physiologic and pathologic inquiries have included the following: the effect of respiratory movements on the flow of lymph under normal and pathologic conditions; the effects of irritants and inflammation on lymph flow; the time relationships and pathways for the removal of inflammatory exudates from the alveoli, pleural and peritoneal cavities; the effects of anoxia on the production of pulmonary edema; the passage of pathogenic microorganisms through the alveolar membrane into the lymphatics; and the role of the lymphatics in pulmonary edema of inflammatory origin, to give a partial listing. A brief recapitulation of the anatomical pathways for the drainage of lymph from the heart and lungs will be given subsequently. For a fuller discussion of any of these subjects, the reader is referred to the literature [*1–7,9–14,17, 20–23*].

The technic, however, of measuring lymph flow from the right duct has been so demanding that it has not been widely used. Drinker and co-workers state "Cannulation of the right lymphatic duct has been a difficult task and is accomplished satisfactorily in about one out of five animals" [*22*]. The possible importance of pulmonary lymph flow, particularly in relationship to certain phases of cardiopulmonary physiology, urges its exact and frequent measurement. Therefore the anatomy of the right lymphatic duct and a practical, relatively simple method of collection and measurement of the lymph flow in it, appear to be important matters for further study. The present paper concerns itself with these two subjects.

LYMPHATICS OF LUNGS AND PATHWAY FOR DRAINAGE INTO VENOUS SYSTEM

The alveoli and atria of the lungs, the actual respiratory parts, do not have lymph ducts surrounding them [*8,17*]. The lymphatics end around the alveolar ducts and do not extend to the alveoli. Free alveolar fluid (e.g., pulmonary edema), which always contains some plasma protein, is removed by (1) the bronchioles and bronchi from which it is coughed up, (2) absorption of proteins, water and salts into the lung lymphatics and re-entrance into the blood thusly, and (3) absorption into the alveolar capillaries of proteins which may be broken down by enzymes into smaller molecules, water and simple salts.

The lungs contain numerous and large lymphatic vessels. Miller [*17*] has pointed out that the lungs are more extensively equipped with lymphatics than are the kidneys or liver. The flow of lymph is generally toward the root of the lungs, judging by the position of the valves in the lymphatic vessels. A plexus of lymphatics accompanies the bronchi and bronchioles and arteries and arterioles of the lungs. These communicate with a somewhat separate group of lymphatics along the pulmonary veins. There is a profuse network of lymphatics in the pleura. These communicate freely with the lymphatics along the pulmonary veins so that eventually the lymph flow in the pleural channels reaches the root of the lungs

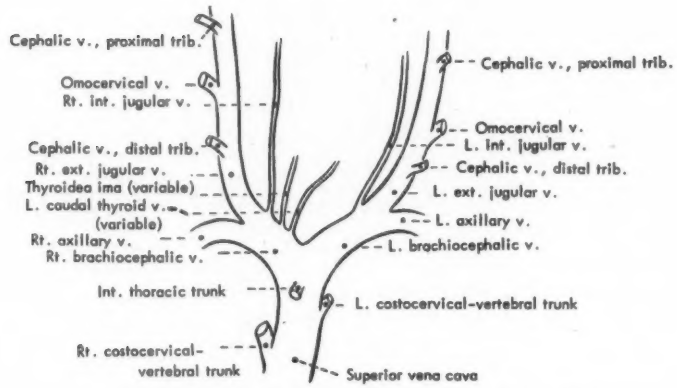

FIG. 1. The veins of the cervicothoracic region in the dog.

where the deep lymphatics converge on the hilar nodes. Lymph nodes are much more plentiful in man than in animals. From the hilar nodes multiple lymph channels enter lymph nodes which lie upon the surface of the trachea between the superior vena cava and the aorta. A separate lymph duct from the heart passes to the upper node in this location. A fairly constant lymph node is located just below the right subclavian vein from which the right lymphatic duct arises.

The lymphatics contain unicuspid or bicuspid valves. Their significance lies in the determination of the direction of lymph flow when the vessels are compressed by muscular contraction or the respiratory movements of the lung [*16*]. The valves in the lymphatics in the parenchyma of the lung are not numerous and readily become incompetent. Blockage of lymphatics in the lung leads slowly to the deposition of fibrous tissue.

The lymph from the right and left lungs, except for a portion at the left apex, drains via the right lymphatic duct into the right subclavian vein [*10,18,19*]. The upper part of the left lung drains into the thoracic duct. The right duct, both in man and in animals, is an exceedingly short and small vessel or group of vessels, and thus a definite bottleneck at the end of a widespread system of lymphatic vessels.

There are anastomotic connections between the right duct and the thoracic duct. This occurred in twelve of twenty-five carefully injected animals described by Freeman [*15*]. Warren, Peterson and Drinker [*22*] state that in about half their dogs, lymph from the right duct contained chyle. Drinker [*10*] states that in 50 per cent of dogs the right lymphatic duct contains chyle, evidence of anastomosis with the thoracic duct. The right duct receives small contributions from the liver and the right side of the thoracic cage, but in the quiescent, anesthetized dog the amount of lymph collected from the right duct expresses the lymph flow from the heart and lungs since these organs are active. The lymph flow from the cervical and brachial trunks is extremely small in the absence of muscular contractions.

ANATOMY OF THE RIGHT LYMPHATIC DUCT IN DOGS

The venous channels of the right cervicothoracic region are illustrated in Figure 1 which is a useful guide for the dissection of this area.

The thoracic duct and the right lymphatic duct usually enter the jugular or subclavian veins at or near their junction on the left and right sides, respectively. The cervical duct and subclavian duct, together with the mediastinal or right lymphatic duct on the right side and the thoracic duct on the left side, enter the venous system in close association with each other, but the arrangement is extremely variable. The right duct often consists of many small ducts. Sometimes it crosses over to the left side.

In the region of the junction of the right subclavian and external jugular veins and the junction of the internal and external jugular veins, numerous lymphatic channels may be seen when stained with Evans blue dye. Unless they contain dye, all but the larger channels are

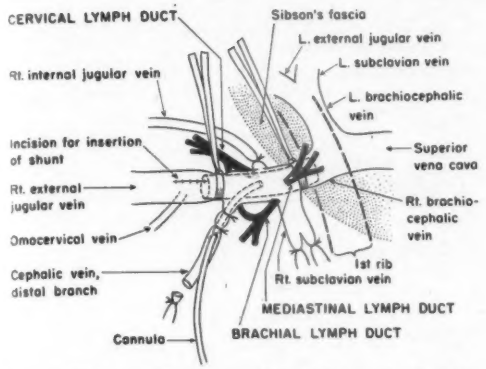

FIG. 2. Diagram of anatomy of the right cervicothoracic region of the dog. The three major lymphatic trunks empty into the region where the subclavian and internal jugular veins join the external jugular vein. The position of the plastic tube in the external jugular vein is indicated.

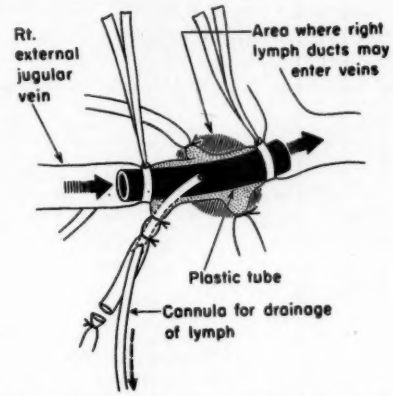

FIG. 3. Drawing to illustrate the method of creating chamber to collect lymph from the right duct. The chamber is drained by a small bore plastic tube passed through the cephalic vein.

almost invisible since they are extremely small and are surrounded by fat and areolar tissue. A number of channels enter the veins from behind and from the left side, although most enter the right side. They will be injured by even a meticulous dissection if an attempt is made to isolate them.

The anatomy of the right cervicothoracic region is illustrated diagramatically in Figure 2. This shows the general arrangement of the three major lymph channels (i.e., cervical, brachial and mediastinal or right lymphatic ducts), where they enter the jugular-subclavian vein area. As previously described, the right lymph duct is extremely variable, and numerous tiny ducts are the rule.

To illustrate how variable the right lymphatic duct may be in its entrance into the venous system, the following brief analysis of forty-seven dissections is given. In our experience, although a single duct often enters the vein, rather than multiple channels with separate openings, this duct usually has several tributaries—generally two or three—which join to form the terminal small, short duct. Undoubtedly in a number of instances additional small channels were overlooked in the dissections. In twenty-seven dogs a single right lymphatic duct was observed, while in nineteen two separate ducts were seen entering the veins. One dog had one larger lymphatic trunk and several small ducts entering the vein separately. In the first group of twenty-seven dogs with a single right duct, nine entered the external jugular vein near the junction of the subclavian vein; eight entered at the junction of the subclavian and external jugular vein; six entered at the junction of the internal and external jugular vein; two entered the internal jugular vein, and one each entered the subclavian vein and inferior vena cava.

In the second group of nineteen dogs with double right ducts, there were eight with one duct which entered the junction of the subclavian and external jugular veins; the other duct entered at the junction of the internal and external jugular veins. Eight had both ducts entering the external jugular vein at different locations. Two had one duct entering the external jugular vein and one entering the junction of the external jugular vein and subclavian vein. In one instance one duct entered the brachiocephalic vein, and the other entered the junction of the internal and external jugular veins.

In a few instances the right lymphatic trunk joined the cervical lymph trunk before entering the vein.

METHOD OF COLLECTING LYMPH FROM THE RIGHT LYMPHATIC DUCT

The technic consists of creating an artificial chamber within the internal and external jugular and subclavian veins in the vicinity of the entrance of the right lymphatic channels. The chamber is created by introducing a seg-

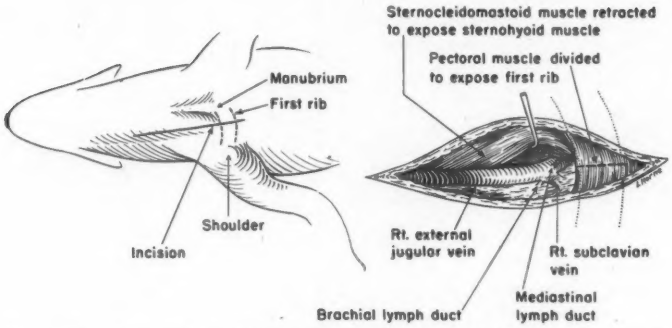

FIG. 4. Drawings to show skin incision and dissection of external jugular vein for studies on lymph flow from the right duct.

ment of plastic tubing into the external jugular vein and ligating it in place. The chamber is formed between the outer wall of the plastic tube and the inner wall of the vein. The lymph drainage collects in the chamber and is drawn off by a small bore plastic catheter inserted into the chamber. (Fig. 3.)

The animals are anesthetized with sodium pentobarbital administered intravenously. Evans blue dye (T1824) is instilled into the right bronchus in order to make the right lymph ducts more easily seen. Eight to twelve cubic centimeters of a 2 per cent solution is injected through a plastic catheter inserted through the trachea into the region of the right mainstem bronchus, the dog lying on its right side.

The animal is then placed in a supine position and the right cervicothoracic region shaved, washed, treated with antiseptic solution and draped. A vertical incision is employed beginning over the medial border of the right sternomastoid muscle and extending into the pectoral region. (Fig. 4.) The external jugular vein is exposed in the lower cervical region and carefully dissected downward, exposing the following structures: the omocervical vein, cephalic vein and internal jugular vein which are tributaries of the external jugular vein; the subclavian vein which is bifurcated or occasionally trifurcated, and the distal portion of the right brachiocephalic vein. Care is taken to preserve the many lymphatic channels in this area.

The tributaries of the external jugular vein are ligated and divided, except the cephalic vein which is conveniently located for insertion of a small bore plastic catheter which taps the chamber. The internal jugular vein and subclavian vein are ligated about 1 cm. from their junction in order to preserve lymphatic channels.

A longitudinal incision is made in the external jugular vein, and a stiff plastic tube about 7 cm. in length, with a diameter approximating the internal diameter of the external jugular vein, is inserted. The distal end of this tubing must lie well in the right brachiocephalic vein proximal to the junction of the right subclavian vein, to avoid obstruction of the lymphatic duct openings by valve leaflets which lie in the lumen of the external jugular vein near the opening of the subclavian vein. The right lymphatic ducts often open into the external jugular vein behind the valve leaflets. This tube is firmly ligated in place with umbilical tapes. The external jugular venous flow passes through the tube without obstruction. (Fig. 3.)

A small bore polythene catheter is inserted through the cephalic vein into the chamber and is ligated in place. The pocket containing lymph and blood is irrigated with a dilute solution of heparin. The plastic catheter then serves as an outflow for the lymph. Immediately after irrigation, the flow of lymph begins. It is stained blue and usually is clear. When the lymph is cloudy, it indicates that lymph from the thoracic duct is crossing over to the right lymph duct.

The method devised has the following advantages: (1) It eliminates the need for cannulating small ducts. (2) The entire lymph flow from the right duct is obtained rather than only that from a single small channel. (3) Opening of the thorax is eliminated. (4) Local anesthesia may be employed if desired. (5) It is applicable to

most dogs regardless of the anatomic variations and anomalies of the right duct.

For measuring the flow of lymph, samples were collected at fifteen-minute intervals. To prevent clotting, small amounts of heparin solution were employed.

When the animals were sacrificed, the lungs were examined to determine the distribution of the blue dye and the weight of the heart and lungs. Specimens were obtained for histologic study when indicated.

RESULTS

In preliminary studies, attempts were made to cannulate the right lymphatic duct by the conventional technic [21]. Dissections were made with the aid of a binocular microscope, and fine bore plastic tubing drawn out to a narrow caliber was used for cannulation. In eighteen attempts, there were four successes or 24 per cent. This figure compares with that of about 20 per cent reported by Warren, Peterson and Drinker [22].

Using the artificial chamber technic, there were fifteen successes in the first consecutive experiments in which this method was employed, or 75 per cent successful attempts. With continued familiarity with the method, this rather surprising figure has been improved and approaches 80 per cent. The five failures were due to failure of lymph to enter the pocket in two cases, accidental tear of the lymphatics in one and failure to tie off venous tributaries which entered the pocket in one. In one the cause of failure was unknown. Failure of lymph to enter the chamber is due to obstruction of the openings of the lymphatics into the vein by clots or by venous valves which seal off the openings when the umbilical tape ligatures impinge on the valves.

The rate of lymph flow, pressure, chemical and cytologic constituents under normal and pathologic conditions will be presented in subsequent communications.

SUMMARY

1. A brief review of the present status of studies of the lymph flow of the lung is presented.

2. A new method for measuring the lymph flow from the right lymphatic duct is described in detail.

3. The advantages of the method are chiefly its simplicity and applicability to most animals regardless of the numerous variations and anomalies of the right lymphatic duct.

4. The anatomy of the right lymphatic duct and some of its variations are described.

Acknowledgment: We are indebted for the drawing and nomenclature of Figure 1 to Malcolm E. Miller, D.V.M., PH.D., Professor and Head of the Department of Veterinary Anatomy, New York State Veterinary College at Cornell University.

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DISCUSSION

Roy Cohn (San Francisco, Calif.): Any method which will permit the accurate study of lymph flow will open an enormous field for further study of the metabolic and fluid processes of the body as well as the spread of disease. Of the many examples that can be cited, I will mention only one, the spread of carcinoma. It is well known that the pulmonary lymphatics arise from right and left jugular sacs and the retroperitoneal lymph sac. The jugular lymph sacs grow down on either side of the trachea to the lungs. The left grows faster than the right, joining with it at the tracheal bifurcation and sends a large contribution to the right lung as well as the left lung. There are several lymph vessels which arise from the cephalic portion of the retroperitoneal sac, which apparently go into the lungs. Some authors believe that these connections account for the early spread to the abdomen of carcinoma of the lower lobes of the lung and hence its well known poor prognosis.

Accurate means of collecting the lymph before it enters the veins may not only allow a better understanding of routes of spread, but also help settle the question of the viability of cells which enter the lymphatics, a problem which has been emphasized recently by Dr. Cole.

I hope that the next report from Dr. Leeds and his group will be a clinical study.

Sanford E. Leeds (closing): I wish to thank Dr. Cohn for being kind enough to discuss this paper. If the method is used by others as successfully as by us, it should expedite the investigation of the function of the lymphatics of the heart and lungs. It is conceivable that the method with some minor modifications could be applied to human patients. Here it might be of value in determining the function of the lymphatics not only in inflammatory disease of the lung but in circulatory problems such as pulmonary hypertension and in other problems such as emphysema.

It would be of great value in the study of cancer of the lung and in unraveling some of the pathways of metastasis.

Studies on Mammalian Homotransplants of Skin

III. AN ATTEMPT TO INDUCE TOLERANCE ACROSS THE PLACENTA IN RATS WITH RNA AND DNA

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OUR previous studies have indicated that tolerance may be induced with pooled blood antigens [1] and with certain nuclear and cytoplasmic components [2]. Billingham et al. [3] reported that desoxyribonucleic acid (DNA) was implicated in the phenomenon of skin transplantation immunity while ribonucleic acid (RNA) was not.

Later, these authors [4] stated that DNA may not necessarily be an essential component of the antigen required to create transplantation immunity. They pointed out that their new evidence suggested that the determinant groups of transplantation antigens were related to the human blood group substances (amino acid polysaccharide complexes). These so-called contaminants might even be present in supposedly highly purified DNA proteins. Snell [5] also mentioned that the enhancing as well as sensitizing antigens may be of a mucoid nature, differing only in subsidiary molecular attachments. Billingham et al. [3] also reiterated the fact that enhancing antigens have long been known to exist in cellular cytoplasmic particles, while his experience indicated that sensitizing antigens did not. He agreed with Snell [5] in that the DNA protein may act as the adjuvant or vehicle for the antigenic material present in nuclear fragments. This, he believed, would explain the destructive action of DNAase to the transplantation immunity reaction.

Sterzl and Hrubesová [6], quoted by Egdahl [7], found that subcellular particles from an immunized homologous donor would transfer antibody-forming ability to five-day old rabbits. They thought that neither antigen nor mature antibodies were present in the transferred material and that the mitochondria, as well as the DNA and RNA protein nuclear fractions, were the effective antibody producers. Campbell [8] disagreed with this theory. He believed that antigen must persist for each molecule of antibody formed. Burnet and Fenner [9] theorized that intracellular enzymes are altered by antigen and produce antibody upon future exposure.

The studies of Washburn [10] indicated that during wound healing in rats, there is an increased concentration of RNA in the cytoplasm of the cells of the basal and lower stratum spinosum layers of the skin. This is also true of human cultured epithelial cells of the deeper skin layers in which mitotic evidence of proliferation occurs. The DNA concentration of cellular nuclei in both healing burned tissue and human tissue culture did not seem to vary. Washburn also stated that the RNA and DNA metabolism of epithelial cells during *in vivo* wound healing and *in vitro* cultures appeared to be identical.

With this in mind, a group of experiments were initiated in which pregnant rats were injected intracardially with RNA and DNA in an attempt to cross the placental barrier and possibly to induce prolonged tolerance in the offspring. In two additional groups of pregnant animals, radioactive labelled RNA C^{14} and DNA C^{14}, respectively, were injected in an attempt to verify the passage of the nuclear and

cytoplasmic components across the placental barrier.

MATERIAL AND METHODS

The experimental animals used were rats of the Long Evans and Wistar strains. Homografts measuring 3 by 5 cm. were exchanged and rotated, thus reversing the hair line to facilitate easy identification. The grafts were observed grossly to determine the onset of slough.

Preparation of RNA and DNA. Ribonucleic acid: RNA was prepared for injection from organs of Long Evans or Wistar rats by the method described by Colter and Brown [*11*].

C^{14}-labelled RNA: C^{14} sodium formate (specific activity of 8 mc./mM.) obtained from the California Corporation for Biochemical Research was dissolved in physiological saline. Aliquots of 0.5 cc. were plated on planchets and counted in a gas flow counter for radioactivity. Doses of 0.55 cc. of this solution were injected intraperitoneally into Long Evans rats weighing 130 gm. each. Similarly, glycine-l-C^{14} (specific activity 1 mc./mM.) was dissolved in physiological saline and injected into other rats. The radioactive carbon label from formate and glycine is incorporated into the purines which are found in both RNA and DNA. Some of the animals were sacrificed after four hours, and the remainder after twenty-four hours. The liver, spleen, and thymus were removed and promptly frozen until needed. The radioactive RNA was extracted by the usual procedure and 1 cc. of solution was plated on aluminum planchets and counted. The radioactivity found was slight. Doses of 0.5 cc. of the radioactive RNA solution from the twenty-four hour samples were injected intracardially into pregnant female rats.

Desoxyribonucleic acid: DNA was prepared from the liver, spleen and thymus of rats of the Long Evans strain by the method of Simmons [*12*].

C^{14}-labelled DNA: Radioactive DNA was extracted by the procedure mentioned from the residue of the first centrifugation after homogenization of the organs removed from rats injected with C^{14} sodium formate.

Analysis for Radioactivity. Animals were sacrificed at various intervals after the injection of radioactive RNA. The rats were anesthetized and a blood sample was taken. The fetus and liver were then removed from the pregnant animals. The fetus was homogenized (20 per cent w/v) in distilled water, using a Waring blender at full speed for five minutes. The maternal liver was also homogenized in the same manner. The homogenates were centrifuged for thirty minutes at 2,500 r.p.m. and the supernatant removed. The supernatant solution was treated with 20 per cent perchloric acid, and after standing in the cold overnight, was centrifuged for fifteen minutes at 2,000 r.p.m. This supernatant and the precipitate were treated separately and aliquots plated on planchets for counting in a gas flow counter to detect radioactivity.

Experiment 1. Ten rats, twenty days pregnant, were injected intracardially with 0.3 to 0.4 cc. of RNA extracted from the antigen donor pool. In every case, the Long Evans rats received RNA from the Wistar rats and *vice versa*. The offspring were grafted with skin from animals of the same strain as the RNA donors at twenty, thirty, and forty days.

Experiment 2. Again, ten rats, twenty days pregnant, were injected intracardially with 0.3 to 0.4 cc. of DNA extracted from an antigen donor pool similar to that described in experiment 1. The injections of DNA were again from the opposite strain of rat. The offspring were grafted at twenty, thirty, and forty days of age with skin from animals of the same strain as the DNA donors.

Experiment 3. Four Long Evans rats and two Wistar rats, sixteen to seventeen days pregnant, were injected with 0.5 cc. of radioactive RNA by the intracardiac route. Twenty hours later, the fetuses, the maternal liver, the spleen, and a blood sample from the mother were taken for analysis of radioactivity.

Experiment 4. The same procedures as described in experiment 3 were repeated using C^{14}-labelled DNA. The activity of the injected radioactive DNA was 558 c.p.m./ml.

RESULTS AND DISCUSSION

In experiment 1, it will be noted (Fig. 1) that the animals grafted at twenty days showed an 18 per cent take forty days after graft (Fig. 2); a 14 per cent take fifty days after; and a 9 per cent take sixty days after. The animals grafted at thirty days showed a 6 per cent take thirty days after graft, and a 4 per cent take sixty days after. At this age interval, the percentage take of grafts in the experimental group (rats receiving the RNA as fetuses) was lower than in the donors. (Fig. 3.) The animals grafted at forty

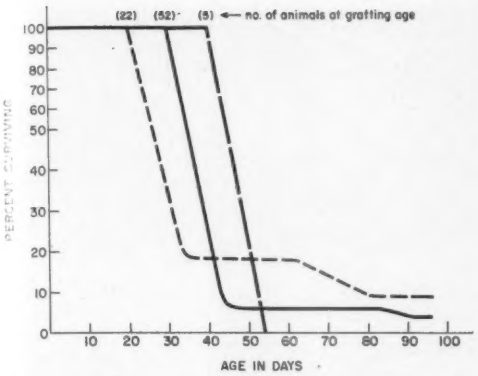

FIG. 1. Graph illustrating percentage survival of grafts applied at twenty, thirty, and forty days of age to RNA recipients.

days had no appreciable take after a fourteen day period and the corresponding donor rats showed a similar percentage of takes.

In experiment 2 (Figs. 4 and 5), the twenty-day group of animals showed only a slightly higher percentage take (Fig. 6) than the control group. (Fig. 7.) The animals grafted at thirty and forty days revealed a 0 percentage take after fourteen days.

In experiment 3, the RNA C^{14} activity found in the fetuses was just slightly higher than the background count.

In experiment 4, the radioactivity found in the fetuses was 500 c.p.m./ml.

At the present time, relatively few samples have been run to show that the RNA and DNA preparations injected are actually crossing the

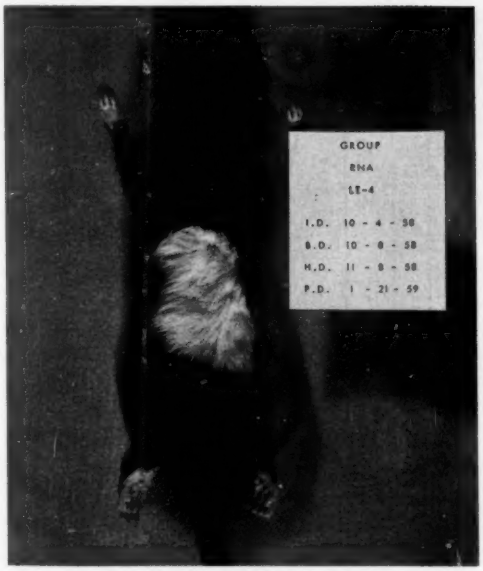

FIG. 2. Photograph of well healed seventy-plus day old homograft in place (RNA injected into pregnant female four days prior to birth).

placental barrier. The slight amount of radioactivity found in the fetuses after RNA injections could be accounted for by the low radioactivity of the injected RNA and its consequent dilution in the mother and fetuses to a level just above background count. The data of experiment 1 indicate that the RNA is producing some effect in increasing the tolerance of the experimental animals over that of the control animals. The radioactivity noted in the fetal samples

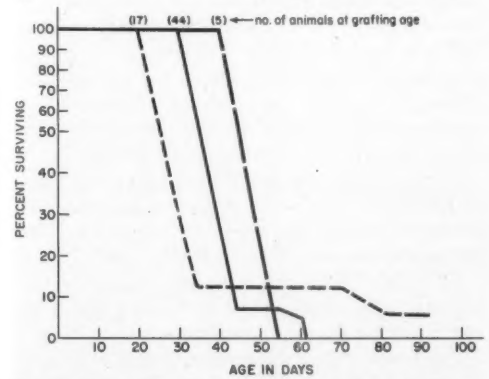

FIG. 3. Graph illustrating percentage survival of grafts applied to RNA donors at twenty, thirty, and forty days of age.

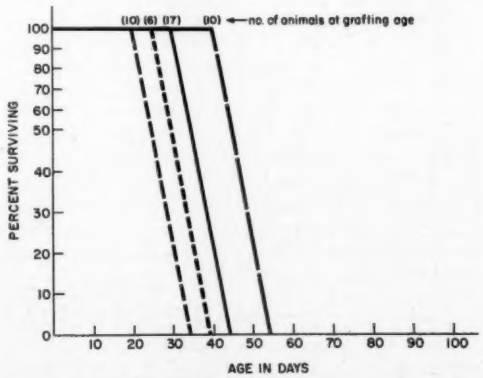

FIG. 4. Graph illustrating percentage survival of grafts applied at twenty, thirty, and forty days of age to DNA recipients.

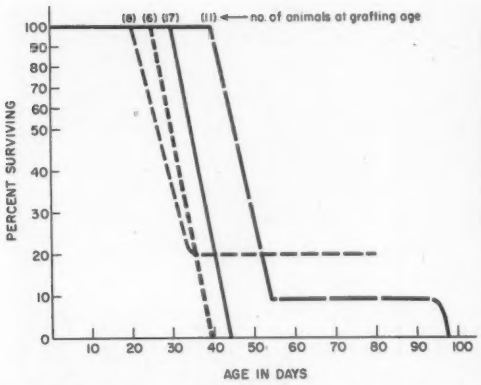

FIG. 5. Graph illustrating percentage survival of grafts applied to DNA donors at twenty, thirty, and forty days of age.

after injection of DNA C^{14} is in accord with the tolerance-producing effect of DNA observed in experiment 2. A comparison of the tolerance effect of RNA and DNA found in experiments 1 and 2 shows that RNA is more effective, and would suggest that for nucleic acids of equal activity, more radioactivity would be found in the fetal samples from rats injected with labelled RNA. Experiments are under way at present to elucidate this point.

The interesting point brought out by the first two experiments is that the skin grafts on the donor animals had as high, or a higher, percentage of takes than that of the experimental animals. This suggests a possible twofold role of the nucleic acids: (1) as templates for self-reproduction and elaboration of proteins which would not cause an immune response in the donor animal when grafted; and (2) as a predominant donor antigen in the induction of tolerance in the fetus. The results of the grafts on animals injected with RNA indicate this postulated twofold role; while the DNA data indicate that the template action predominates. This follows the postulation that the replication of DNA in the nucleus occurs at much higher rates in the fetus than in the newborn or more mature animals. It is known that during fetal development, there is a greater production of DNA in order to keep cellular division and growth at the maximum level while cytoplasmic RNA is required in greater quantities in neonatal and postnatal life for the biosynthesis of cytoplasmic and extracellular protein.

FIG. 6. Photograph of well healed homograft at three months on DNA donor.

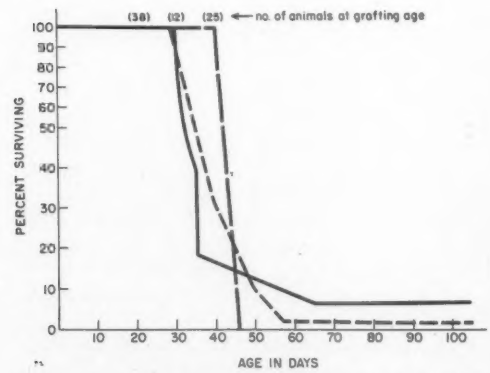

FIG. 7. Graph illustrating percentage survival of grafts applied to control animals at twenty-eight, thirty, and forty days of age. (Previous control animals grafted at twenty and twenty-two days of age.)

At present, we are pursuing our investigation of DNA as a possible stimulus for tolerance induction in neonatal animals as shown in similar former studies utilizing RNA.

Further experiments are underway to determine the optimum quantities of DNA and RNA which are necessary to produce tolerance, both in the fetus and in neonatal animals. Multiple injections are also planned, to prolong or enhance tolerance already induced, or to induce it in previously less successful experiments.

SUMMARY

A review of the more pertinent aspects of work pertaining to the present study as performed by others and by us is outlined.

Four experiments are presented which represent our preliminary efforts to induce tolerance across the placental membrane in rats. In the first experiment, RNA was used and the results were slightly encouraging in that 18 per cent of the graft took in the twenty-day old animals (age of grafting) which represents a significant increase over the control animals (8 to 9 per cent). In the second experiment with DNA as the injected material, the difference between the percentage take of the treated animals and the control animals was negligible. Experiments 3 and 4 involved the use of DNA and RNA tagged with C^{14}, in an effort to determine the quantity which actually entered the fetus through the placenta. This phase of the work is encouraging in that significant quantities of C^{14} were counted in the fetuses, thus indicating passage of these cellular components.

In view of our previous findings that tolerance may be produced by injecting RNA intracardially into neonatal rats and our present findings that the injected substances (DNA and RNA) crossed the placenta, we are hopeful of more significant results in future experiments with increased and repeated injections of modified antigen.

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DISCUSSION

William P. Longmire, Jr. (Los Angeles, Calif.): This interesting work presented by Dr. Ashley represents an important basic contribution to the effort of unraveling certain aspects of the homograft problem. Based on some earlier observations of Medawar on the enhancement of immunity, he has shown for the first time that the inert proteins, DNA and RNA, when injected into newborn rats, will produce tolerance to subsequent homografts. Additional experiments indicate that these materials pass the placental barrier in pregnant rats and at least RNA protein seems to produce some degree of tolerance in the fetus. These investigations, of course, involve complex chemical technics and it is difficult, if not impossible, to be certain that one is dealing with chemically pure active materials, and that the C^{14} found in the fetus is still attached to the materials as originally injected. In any event, it is a most interesting approach to the problems of possible production of the phenomena of tolerance in man. Whereas the period during which tolerance may be produced in the rat persists for several days after birth, this period in man is probably confined to about the first trimester of pregnancy. Therefore, if tolerance can be produced in man, it will probably depend upon finding some substance capable of producing tolerance which will also pass across the placental barrier. RNA protein might possibly prove to be such a substance.

Similar work in the chick, performed by Dr. Paul Terasaki in our laboratory, has demonstrated that tolerance is not individually specific but that chick embryos injected with pooled blood may be made tolerant to subsequent skin homografts from

unrelated chicks. In attempts to track down the substance responsible for producing tolerance in chicks, Dr. Terasaki has also found that intact lymphocytes, monocytes, thymocytes and splenic cells will all produce approximately the same degree of tolerance. However, in his experiments, soluble splenic extracts tried in various doses and injected by various routes all failed to produce tolerance. Terasaki's experiments in the chick would indicate that intact viable cells were necessary for the production of tolerance.

If Dr. Ashley's results can be confirmed, they represent a most important step in the identification of a substance responsible for tissue specificity, and possibly a most important step in the clinical application of homografting. The availability of a soluble antigen such as this would also be of value in providing a means of producing tolerance without, at the same time, producing a graft versus host reaction.

These observations, so briefly presented, represent a vast amount of work and I would like to compliment Dr. Ashley for these original studies in a most important field.

J. Englebert Dunphy (Portland, Ore.): Because I have little grasp of the immune mechanisms in the homotransplant problem, I am keenly aware of the importance of Dr. Ashley's observations. I would ask him if it is not a little surprising that the RNA fraction was more effective than the DNA, which, it would seem to me from my understanding of Medawar's work, might have been more effective.

We have been interested in what is going to happen after Dr. Longmire and Dr. Medawar and others solve the homotransplant problem, because then we will be faced with the opportunity of transplanting tissues, let us say, more or less at will.

We have been studying the effects of autotransplants of bone marrow. There is a good deal of evidence in the literature that bone marrow can be successfully homotransplanted, but the evidence rests upon discovering and recognizing cells in the blood stream. We have been trying to transplant bone marrow, whole marrow, to a site where we could study it, and have found that in the dog, if one takes the rib and splits it longitudinally and sharpens the end, it can be threaded neatly into the spleen, and when examined at the end of a period of six weeks, one finds completely normal, healthy bone marrow.

However if one examines the autotransplant of bone sequentially the marrow completely disappeares in a period of about six to eight days. The only tissue which remains in this marrow is a primitive large cell which the hematologists tell us may be a precusor cell from which in the next three weeks there is a complete regeneration of marrow. I would suspect, therefore, that in homotransplanted bone marrow one would expect a similar rapid destruction of the transplanted cell and a period of at least several weeks before this primitive cell, if it can be produced by a homotransplant, will then regenerate enough bone marrow to produce a variety of new cells.

Franklin L. Ashley (closing): The more we read and the more we observe concerning this problem the more confused we are. There is one possible explanation for Dr. Dunphy's question and that has been supported by the work of Washburn in that we believe that in the fetus DNA is the predominant factor in protein metabolism, that is the nuclear elements of the cell, but in the postnatal protein metabolism we think RNA may become more important, this being the cytoplasmic element. This possibly may explain why RNA so far has been more effective. However, we are going to change our DNA preparation a little, try to modify the solution and preserve the histone covering to ascertain whether this will change our DNA results. We are also going to try multiple injections, and we have a technic whereby we can cannulate the thoracic duct in a rat and obtain almost pure lymphocytes and monocytes. We will use these pure cells in an attempt to try to extract DNA and RNA from them.

Gastric Adenomas

A CLINICOPATHOLOGIC STUDY OF SEVENTEEN CASES

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To the twentieth century student of surgery who knows of the original description of a gastric polyp given in 1557 by Amatus Lusitanus [1], and is familiar with the literature on this subject for the ensuing four hundred years, the analysis of a series such as this may appear repetitious. The skills, technics, and equipment used in the roentgenologic diagnosis of gastric polyps have been so modified in the past decade, however, that these supposedly rare tumors are now frequently recognized during routine upper gastrointestinal roentgenographic studies. The fact that nearly half of the seventeen cases in this series, which cover a seventeen-year period at St. Vincent Hospital, occurred during the past two years, and were correctly diagnosed preoperatively, may well be an indication that these neoplasms are not nearly as uncommon as has been thought. A consideration of the clinical and pathological features, radiologic diagnosis, and surgical management of these lesions, therefore, seems timely.

For the purposes of this study, gastric adenomas have been defined as epithelial neoplasms composed largely of mucous-secreting glands which arise from the gastric mucosa and extend into the lumen as polyps of varying size. They occur most frequently in the pyloric antrum, but may be found in any part of the stomach. They may be sessile or pedunculated, single or multiple, and sometimes confluent. Leiomyomas, lipomas, and other tumors of mesodermal origin, any of which may occasionally form intraluminal polypoid masses, have been excluded, as have such non-neoplastic lesions as heterotopic pancreas and so-called gastritis polyposis (chronic hypertrophic gastritis) that sometimes simulate new growths.

HISTORICAL REVIEW

In 1835 Jean Baptiste Cruveilhier [2] described the complications that may develop from the polyps blocking action of the pylorus when these polyps attain a certain size and are pedunculated, and he commented on their tendency to undergo malignant change. The earlier students of this problem [15] offered histological evidence in support of the concept that these tumors were the result of chronic gastritis. During the last fifty years, however, much attention has been directed to the study of these polyps as potential premalignant lesions. In 1908 Max Versé [3] described cases in which polyps that appeared to be the result of chronic gastritis initially, eventually became malignant. The first instance in which a gastric polyp was demonstrated radiologically was reported in 1911 by Heinz [4,18]. He observed the presence of a many processed shadow hanging by a stalk from the lesser curvature of the stomach on fluoroscopic examination. The diagnosis was confirmed by Fritz de Quervain who subsequently resected the tumors. In 1912, the first roentgenogram showing a gastric polyp was produced by Jesse S. Myer [16]. The plate was taken about fifteen minutes after the ingestion of 1½ ounces of bismuth in a pint of sour milk. Ten years later, Rudolf Schindler [6] reported that he had visualized a gastric polyp through the rigid gastroscope.

In 1947, Paul and Logan [7] stated that the most important aspect of gastric polyps is their tendency to become malignant. In 1950, Moyer and Clayton [8] extended this concept by their belief that "really benign polypoid growths of the stomach are so rare that the

possibility of their existence should never be used as the basis for deferring operative intervention." There has been some disagreement over the relationship between the size of the polyps and malignancy. Mikal and Campbell [9], in a study of eighty-five polyps of the gastrointestinal tract, did not find any correlation. In March 1953, Hay [10,11] extended supporting evidence that the size of the lesion is diagnostic. In his series only one polyp became malignant of eighty-two gastric polyps under 2.0 cm. in diameter. In 1958 Pack [12] stated that the "incidence of gastric cancer has been higher in patients with multiple gastric polyps than in those with single polyps. Single polyps that are less than 2.0 cm. in diameter have been consistently benign."

Many of the adenomas described have been in patients with achlorhydria, and it is believed by some that gastric cancer is prone to develop in such patients. Wangensteen [13] reported in 1951 that the gastric polyp signifies a functional loss of parietal cell secretion. He also stated in this monograph that the gastric polyp does not become malignant as readily as the colic or rectal polyp. Klein and Geller [14] in 1951 described a case in which three similar appearing polyps were found at gastroscopy. When this patient was re-examined two years later it was discovered that one of the polyps had become malignant.

It is apparent, in reviewing the literature, that there is some divergence of opinion in the minds of American surgeons as to the malignant potential of these polyps, and the type of surgical management indicated. The increased frequency and accuracy in the diagnosis of gastric adenoma, brought about by improvement in equipment and procedures, have now forced re-evaluation of the problem of treatment and a better understanding of the relationship, if any, to carcinoma of the stomach.

RADIOLOGIC EXAMINATION AND DIAGNOSIS

A survey of the cases in this series has convinced us that when the stomach is examined by means of barium meal, the radiographic appearance of a gastric adenoma is an accurate reflection of the gross form and pathologic characteristics of the lesion. It is quite likely that the smaller adenomas will not be visible on routine prone oblique and posteroanterior radiograms of the barium-filled stomach, because the dense column of barium hides them. The most rewarding method for demonstration of an adenoma is careful, gradual compression of the stomach under fluoroscopic observation. The shadow of a soft adenoma can be obliterated by too strong a compression, whereas it may be demonstrated clearly if this compression is gradually decreased. Spot roentgenographic views are invaluable as permanent records because they are made with the precise amount of compression necessary and in the exact degree of obliquity required to demonstrate the lesion most clearly. Compression applied by a cone attached to the fluoroscopic screen seems to give more accurate visualization than compression with the lead-gloved hand of the examiner. If the adenoma is pedunculated the extent of mobility and length of the pedicle can be determined by observation during compression maneuvers under the fluoroscope.

The shadow of an adenoma is characterized by a sharply defined margin at the junction with the neighboring barium. The lesion may be round, multilobulated or pedunculated. An intramural lesion such as leiomyoma, lipoma, or heterotopic pancreatic tissue may produce a radiolucent shadow, but there will be a gradual "gray" transition zone at the edges of the lesion, in contradistinction to the sharp delineation of the mucosal adenomatous lesion. Gastric polyps with very long pedicles may prolapse through the pylorus into the duodenal bulb where the head of the polyp is frequently first encountered; in this situation the alert radiologist will attempt to determine whether the space-occupying lesion visualized is primary in the duodenum or has prolapsed from the stomach.

Differentiation of the histologic type of a polyp by radiologic characteristics is usually not possible although a polypoid leiomyoma with central ulceration usually has a typical appearance. Malignant change in a small lesion is not evident from the roentgenographic appearance. A small papillary carcinoma, moreover, may have an appearance identical to a benign polyp. If the polypoid lesion is associated with evidence of stiffening of the neighboring gastric wall or coarseness of the mucosa, malignant change would be suspected.

In addition to the compression method of demonstration, adenomas may be shown by double contrast methods, utilizing a coating of barium on the mucosa and exposing the mucosal

surfaces thus coated through the air-filled stomach. The swallowed air normally present is often sufficient but may be supplemented, if necessary, by ingestion of a small amount of carbonated beverage. For the double contrast method, the proximal portion of the stomach, including the fundus, cardia and body, is studied with the patient in the erect position so that the barium gravitates into the distal portion. The body may be exposed with double contrast with the patient in the supine position as well, with the left side elevated. The inferior portion of the body of the stomach and the antrum may be studied with double contrast with the patient in the supine position and the patient rotated into the positions necessary to expose the various mucosal surfaces most clearly as the barium gravitates into the superior portion of the body and fundus. The double contrast method is particularly necessary in locating adenomas occurring in the superior portions of the stomach which are not accessible to palpation because of the overlying rib cage. In the remainder of the stomach direct palpation is more likely to demonstrate an adenoma than the double contrast method.

It should be emphasized that the presence of the lesion, especially a small one, may not be appreciated fully until the mucosal surfaces have been visualized several times by repeatedly allowing the barium to fill out the stomach and then thinning the barium column by compression. Artifacts such as air bubbles and accumulation of mucus in the barium must be differentiated from actual lesions.

CLINICAL AND PATHOLOGICAL FEATURES

Seventeen patients with gastric adenomas, with or without other disease of the upper gastrointestinal tract, have undergone surgery at St. Vincent Hospital since 1941. Seven of these patients were diagnosed and treated within the past twenty-four months. All but four were over sixty years of age, the average age being sixty-five. The youngest patient was thirty-eight years old and the oldest was eighty. In contrast to the usually reported preponderance of males in the proportion of approximately 3:2, nine of seventeen patients were females. Fourteen patients were treated by partial or total gastrectomy. There was one resection of the esophagus with the incidental finding of multiple gastric polyps. Local excision of a solitary polyp was performed in one case,

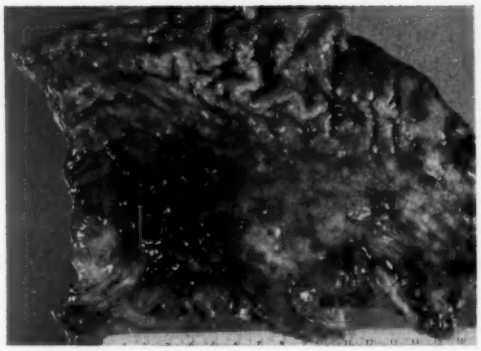

FIG. 1. Mrs. M. S. P. (No. 116012) aged sixty-eight. Gross photograph of stomach resected for massive hemorrhage. A cluster of eight or ten hemorrhagic sessile polyps is present near the lower left hand margin. Not so well shown is an equal number of smaller polyps scattered throughout the fundic and pyloric mucosa.

and a gastrostomy in one case of massive gastrointestinal hemorrhage in a patient who had advanced cirrhosis of the liver. In the latter case, no source of the bleeding was discovered at operation: the patient died of exsanguination, and at autopsy a single adenomatous polyp was found to be the cause. This has been the only death in the series directly attributable to an adenoma, but in two other cases surgery was necessary because of severe hemorrhaging adenomas. (Fig. 1.)

In two cases benign polyps were associated with infiltrating carcinoma of the stomach. Other concomitant conditions encountered included duodenal ulcer, gastric ulcer (Figs. 2 and 3), leiomyoma of the stomach, and islet cell adenoma of the pancreas. Three patients had atrophic gastritis, but in three others there was hypertrophic gastritis. Three patients were operated upon because of diffuse polyposis. In three instances the polyps were considered to be displacing lesions which produced symptoms because of their size or mobility.

During the period encompassed by the study there were two additional cases in which polyps diagnosed by roentgenograms could not be demonstrated at operation. One patient with duodenal ulcer was thought to have a polyp by preoperative roentgenograms but none was demonstrated in the resected stomach. Another was operated upon for cholelithiasis, but no gastric polyp was demonstrated by the surgeon, although one had been described by the radiologist.

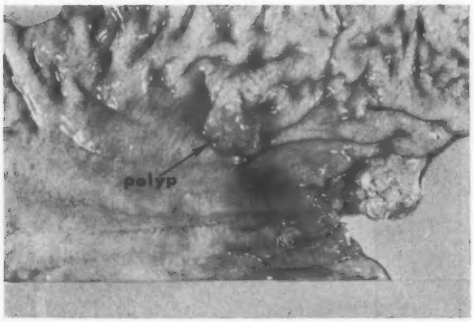

FIG. 2. Mrs. J. C. E., (No. 54208) aged sixty-two. Photograph of surgical specimen showing typical pedunculated adenomatous polyp (arrow); a coexisting peptic ulcer overlying the pylorus is also present.

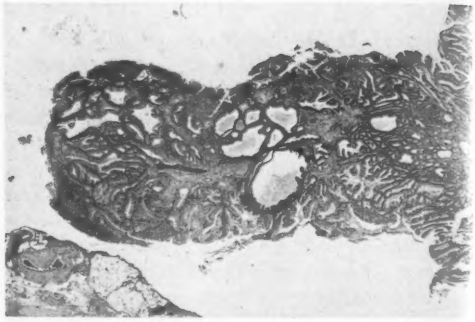

FIG. 3. Same patient. Microscopic section of adenomatous polyp. Note the uniformity of the gland structure. There is superficial ulceration and inflammation at the tip.

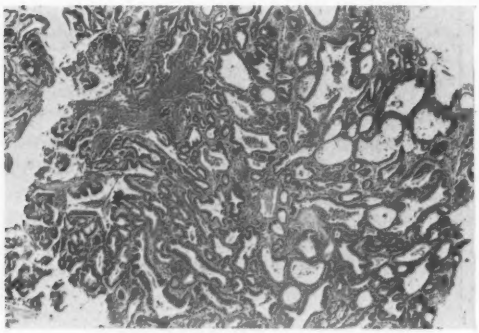

FIG. 4. Mrs. F. B., (No. 163011) aged sixty-seven. Photomicrograph of one field of a 5 cm. polyp. In this and other areas the microscopic structure was benign.

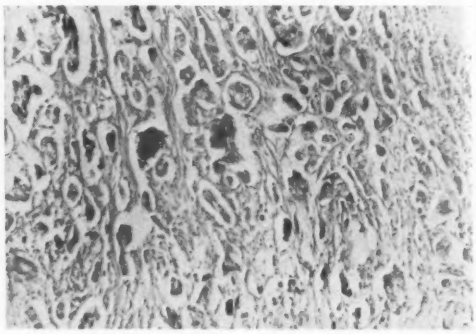

FIG. 5. Same patient. Photomicrograph of another field. In this area the pattern is frankly malignant. Early invasion of the submucosa had occurred.

Review of the pathologic material showed that the polyps occurred with approximately equal frequency on either curvature, and the anterior and posterior walls of the stomach. In fifteen of the seventeen cases the polyps arose in pyloric type mucosa, although they were often found a considerable distance proximal to the pyloric sphincter. In two cases there were small polyps arising from fundic mucosa. Multiple polyps, ranging from as few as two to as many as twenty or more, were found in eight cases, and in one instance almost the entire gastric mucosa was studded with them. They ranged in size from 0.3 to 5 cm. in maximum dimension. Most of the smaller ones were sessile while those over 1 cm. in diameter were often pedunculated.

On microscopic examination, the smallest adenomas were often little more than localized hyperplastic proliferations of mucous-secreting glands. The larger ones were composed predominantly of similar, but often larger glands that had a distinctly neoplastic appearance. In many instances there were papillary formations; microcysts were frequently found in the deeper portions. Usually the lining epithelium of the glands was well differentiated and strikingly uniform, but where superficial erosion and inflammation were present the cells often showed loss of mucous-secreting function and varying degrees of atypia. In most respects, these changes resembled those commonly seen in the superficial portions of colic and rectal polyps. There were no instances in which difficulty was encountered in deciding whether the tumors were benign or malignant. Malignancy was found in only one case (Figs. 4 and 5), the largest polyp in the series. This was a broad based, freely movable lesion that showed no evidence of infiltration on gross examination.

Microscopically, some portions of the lesion had an entirely benign appearance while other areas were atypical, and one focus showed marked anaplasia with frank invasion of the submucosa.

During the period covered by the study, a number of well differentiated polypoid carcinomas of the stomach whose appearance suggested possible origin from pre-existing adenomas were encountered. These were excluded from the series because definite demonstrable evidence of derivation from benign polyps was lacking. We consider the case cited herein to be evidence that malignant transformation of previously benign adenomas does occur, although the series is too small to permit estimation of the incidence.

SUMMARY AND CONCLUSIONS

A study of seventeen patients with gastric adenomas indicates that a high percentage of these tumors can be diagnosed preoperatively with the aid of improved radiologic technics. The lesions are often multiple, and frequently coexist with a variety of other conditions, including peptic ulcer of the stomach or duodenum, gastric carcinoma, and either atrophic or hypertrophic gastritis. They may be complicated by massive hemorrhage, and the distinct possibility of malignant change that is undetectable by radiologic or clinical means exists. These factors, plus the fact that the tumors are located in an organ that is inaccessible to continued direct observation, make subtotal resection of the stomach advisable.

Acknowledgment: We wish to express our thanks to Dr. Milton Hyman for providing us with roentgenograms for several cases and for many valuable suggestions.

DISCUSSION

CARL P. SCHLICKE (Spokane, Wash.): In our experience, gastric adenomas have been uncommon lesions. In the hospital in which I work there are about 24,000 admissions a year; one-fifth of these patients undergo major operations. In the last five years we have seen only two patients with gastric polyps a year. These ten patients include four who were not operated upon because of age, debility or associated disease. However, when one considers that almost half of Dr. Roberts' cases turned up in the last two years of a seventeen-year period, it is quite possible that a more careful search, using some of the methods he describes, would improve our batting average. Seven of our patients were men, three were women. The age distribution was about the same as in Dr. Roberts' cases. Most of our patients complained of indigestion, anorexia and vague epigastric pain. None of them had gross bleeding or symptoms of obstruction. It is of interest to me that for the most part their symptoms were of short duration, measured in terms of weeks, occasionally months, and in only one instance as long as a year. Radiologic diagnoses were: carcinoma, one case; gastric polyps, five cases; uncertain, four cases. In those operated on polyps were multiple in three instances, single in three. Local excision was carried out five times, sleeve resection of the stomach once. This is in marked contrast to Dr. Roberts' fourteen resections and one excision. One patient who had multiple polyps in association with hypertrophic gastritis predominantly involving the proximal third of the stomach underwent a gastrotomy and excision of one polyp and has remained well during the six years that he has been followed up. The symptoms which patients with this condition present may be the compelling reason for operation, but more commonly it is because of anxiety regarding the possibility of malignancy. In general, the larger the lesion the more likely it is to be malignant. The presence of achlorhydria, ulceration, or rapid growth, also suggests malignancy. In one instance a polyp prolapsing through the pylorus into the duodenum proved to be a submucous lipoma. This simply emphasizes the fact that only the pathologist can tell what a given lesion is. Whether these adenomas undergo malignant degeneration, or whether the cases in which malignancy develops are coincidental, is actually of academic interest only because operation is mandatory if the risk is at all acceptable if one cannot exclude malignancy. Yet, as recently as 1952, Yarnis et al., advised conservative therapy for small solitary adenomas, following them up with frequent gastroscopic examinations. Suspicious single adenomas were excised and resection carried out for multiple ones. In a recent publication by Carlson and Ward, some patients were followed up as long as ten to twenty years without operation and no trouble developed. However, 16 per cent of the solitary polyps in these patients were found to be malignant, and more than half of the polyps found to be malignant at operation had been considered benign preoperatively. Since carcinoma may develop after either local excision or resection these cases should be followed up closely. If excision is carried out, it should be wide, and whether excision or resection is performed a careful inspection of the gastric remnant should be carried out before closure. In some patients with multiple polyposis and changes suspicious of malignancy, a total gastrectomy may be necessary.

JOSEPH M. ROBERTS (closing): In a paper by several San Francisco clinicians which was pub-

lished in the December 1958 issue of *Surgery, Gynecology and Obstetrics*, the point is made that the cuff of the stomach which is left following a resection should be examined; in their experience adenomas had been overlooked proximal to the area of excision in a certain percentage of cases. They also reported that malignancies had followed a resection distal to the residual adenomas.

The other observation made by Dr. Schlicke is that the history in this series of patients is rather short and that there is a high incidence of concomitant lesions. These may be explained by the fact that the achlorhydria present in a large percentage of cases may be an expression of an alteration in parietal cell secretion, as suggested by Dr. Wangensteen, and the changes which we find are expressions of this.

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Pseudomyxoma Peritonaei

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UPON opening the peritoneal cavity, it is rather startling to have about 1 gallon of yellow jelly-like material unexpectedly extruded. This is particularly disconcerting when the peritoneal opening happens to be through an inguinal hernia sac. It is a source of additional chagrin when a review of gross pathology and microscopic sections, taken during the course of herniorrhaphy on the opposite side five years earlier, reveals that the intra-abdominal process was fully established at that time.

A seventy year old white man was admitted to Swedish Hospital, Seattle, on February 13, 1953, for repair of a left inguinal hernia the following day. His past medical history was essentially negative for abnormalities. He had noted a lump in the left groin for the past five days, reducible until the day of admission. On examination there was an incarcerated left inguinal hernia of moderate size. The remainder of the physical examination was not remarkable.

At operation the indirect hernia sac was delivered and incised. A piece of partially strangulated great omentum, containing areas of what appeared to be "mucoid degeneration," was amputated. The hernia was repaired and convalescence was uneventful. Microscopic sections of the excised omentum showed chronic granulomatous inflammation and irregular collections of mucin. No evidence of malignancy was noted. (Fig. 1.)

On April 29, 1958, the patient was readmitted to Swedish Hospital for repair of a symptomless right inginal hernia of six months' duration. No provocative lifting or straining could be recalled. There had been no excessive coughing. He had no urinary complaints. Gastrointestinal function had seemed quite normal. There had been no abdominal discomfort and no undue distention had been noted.

Physical examination was unrevealing aside from slight fullness of the abdomen with a peculiar doughy consistency on palpation, and a reducible right inguinal hernia which descended into the scrotum. No abdominal organs or masses could be felt, and there was no tenderness. Rectal examination revealed no abnormalities. Red and white blood

FIG. 1. Mucus embedded in great omentum at first operation. PAS preparation.

FIG. 2. Mucus being extruded through laparotomy incision. Hernial sac elevated on right.

counts, serology and urinalysis were all within normal limits.

At operation on April 30, 1958, the right inguinal canal was opened through a standard incision. When the hernial sac was mobilized it had a peculiar brownish appearance. When the sac was opened approximately 4 quarts of bright yellow gelatinous material was extruded. It contained strands of dense whitish material. The material was too thick to pass through a suction tube and too liquid to pick up in one's hand. The evacuation could only be hastened by pressure on the abdominal wall.

In order to locate the source of the material, the skin incision was extended upward and the peritoneal cavity re-entered through a large transverse muscle-splitting incision with partial division of the rectus sheaths. More of the material was then extruded. (Fig. 2.) Adherent "seedings" of the material were noted on the parietal and visceral peritoneum. The appendix appeared normal in its proximal 2 cm. The distal portion was replaced by a cystic mass about 10 cm. in diameter, densely adherent to the posterior aspect of the abdominal wall. It appeared unruptured. When opened it contained mucinous material similar to that in the free peritoneal cavity. It was thin walled except on its superior aspect where it was about 0.5 cm. thick and had a velvety lining. The great omentum was firmly attached to this area and showed the mucinous deposits seen at the previous operation. The appendix, adjacent sac, and a portion of the great omentum were removed. The upper incision was closed without drainage and the hernia was repaired in a standard manner.

The pathologic diagnosis was ruptured mucocele of the appendix with pseudomyxoma peritonaei. (Figs. 3 and 4.) Convalescence was uncomplicated and the patient has remained quite well until the present time. Abdominal examination has not thus far suggested an increase in the pseudomyxomatous material.

Pseudomyxoma peritonaei, also referred to as "jelly belly," is a curious and relatively rare pathologic process characterized by deposits of pseudomucinous material in the free peritoneal cavity. It was first accurately described by Werth [1] in 1884 in the following words. ". . . the peritoneal cavity in these cases is found filled with gelatinous material in its entire extent. This material is found partly lying free and partly in the form of thick semi-transparent layers lying on and firmly attached to the abdominal wall and intra-abdominal

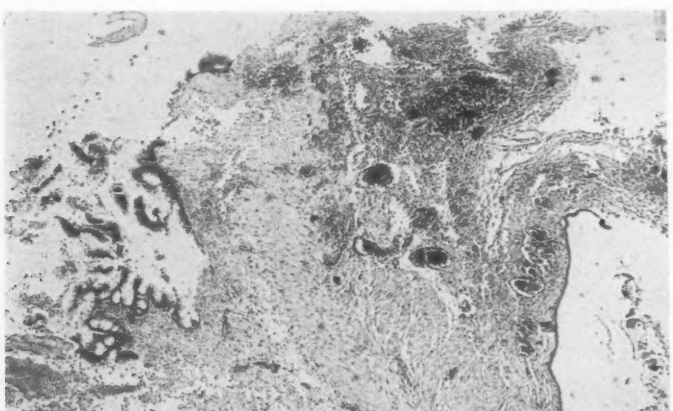

FIG. 3. Wall of mucocele showing papillary folds of appendiceal mucosa. Hematoxylin and eosin stain.

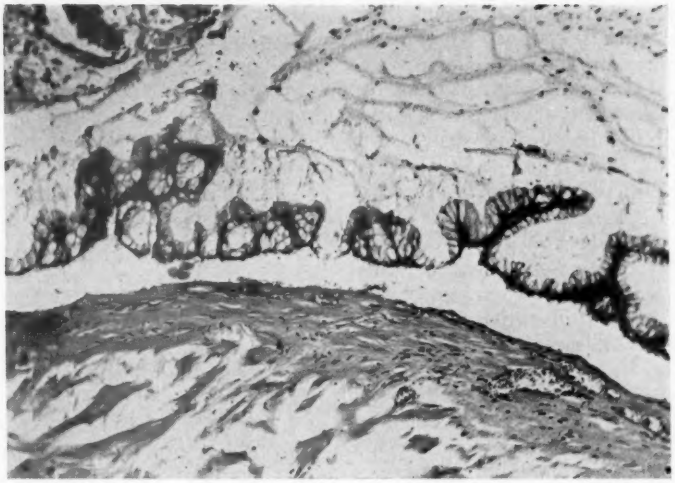

FIG. 4. Mucus secreting cells on peritoneal surface. Hematoxylin and eosin stain.

organs. . . . It is caused by a peculiar reaction of the peritoneum to the jelly-like material which has excaped into the peritoneal cavity by way of spontaneous rupture of ovarian cysts."

Until 1901 the process was thought to be exclusively of ovarian origin. At that time Fraenkel [2] described a case found at autopsy, occurring in a male, secondary to a ruptured mucocele of the appendix. Since then it has been realized that pseudomyxoma peritonaei may arise not only from ruptured appendiceal mucoceles, ovarian cysts and tumors, but also may occur secondary to other conditions such as cecal diverticula, persistent omphalomesenteric ducts and peritoneal cysts. It has also been reported associated with ovarian cystadenoma and appendiceal mucocele in the same patients, resulting in ambiguity as to the primary source and genesis of the peritoneal process in these instances. Hilsabeck and associates [3] concluded that these are instances of simultaneous and independent pseudomucinous cystadenocarcinomas of the appendix and ovary.

That pseudomyxoma peritonaei arising from mucocele of the appendix is somewhat of a rarity is confirmed by Pizzi's [4] review of 2,300 appendectomies in which twelve mucoceles were removed and only one was associated with the myxomatous process. Timoney [5] found four cases of mucocele in 3,087 appendectomies, also with only one case of pseudomyxoma peritonaei. Woodruff and McDonald [6] noted 146 mucoceles in 43,000 appendectomies at the Mayo Clinic. There were only four cases of rupture with intraperitoneal involvement.

Werth believed pseudomyxoma peritonaei to be an exudative inflammatory reaction of the peritoneum to the presence of mucus, a type of non-neoplastic foreign body peritonitis. Subsequently the view was widely held that epithelial cells lining a ruptured cyst were transplanted to the peritoneal surfaces and there took root to continue the secretion of the gelatinous material. Naeslund [7] and Cheng [8] ligated the appendix in rabbits without disturbing the blood supply. They were able to create mucoceles without inciting acute appendicitis. Pseudomyxoma peritonaei subsequently developed in many of the rabbits. The latter condition also resulted when contents of the artificially produced mucoceles were introduced into the peritoneal cavities of normal rabbits.

While well established as terminology for the pathologic process, the term "pseudomyxoma" is probably a misnomer. When the condition was first described, a difference between mucin and pseudomucin was based on the presence or absence of coagulability by alcohol. Since then it has become established that coagulability with alcohol decreases with increasing age of the mucin. Hence, what has been called pseudomucin is simply old mucin [9].

There are some cases of pseudomyxoma peritonaei which are unquestionably malignant, including those secondary to mucoid carcinomas of the intestinal tract and malignant mucinous lesions of the ovaries. Regarding the incidence of malignancy in pseudomyxoma peritonaei of appendiceal origin, there is disagreement. From a clinical standpoint the course often suggests a benign process. Certainly there are instances in which removal of the diseased appendix results in regression of the pseudomyxomatous intraperitoneal masses. The innocuous chronicity that often occurs is well illustrated in the case previously described. Metastases by lymphatic or vascular routes have not been observed.

In spite of these characteristics, Woodruff and McDonald [*10*] concluded that pseudomyxoma peritonaei of appendiceal origin occurs only in those patients in whom formation of a mucocele is associated with grade I adenocarcinoma. They believed that the mucus which may fill the peritoneal cavity in these cases is secreted by malignant cells which have escaped from the original cyst and become implanted. Their notion is subject to wide disparity of opinion among other pathologists. Individual views appear largely governed by the varying cystologic interpretation of the process.

As in the case previously cited, the condition is usually not diagnosed preoperatively. The masses of pseudomyxomatous material accumulate slowly, often over a period of several years. Symptoms depend upon the location and size of such masses. In the advanced state abdominal fullness, pain, constipation, nausea, vomiting, weakness and eventually intestinal obstruction may occur.

Regarding therapy in those cases secondary to mucoceles of the appendix, appendectomy and evacuation of as much of the pseudomyxomatous material as possible is generally advocated. Complete removal is usually impossible. Because of adherence of the material to abdominal viscera, resection of involved bowel or other organs may be indicated. Radiotherapy has not been sufficiently successful to encourage its use. The efficacy of radioactive isotopes has as yet not been evaluated.

It is impossible to give an accurate prognosis in the individual case. There have been some instances in which large amounts of the pseudomucinous material have been allowed to remain in the peritoneal cavity and in which long remissions or apparent cures have occurred. Others, in which much of the material was removed, have ended fatally [*11*]. Because of the rarity of the condition statistical analyses are not abundant. Hilsabeck and associates [*3*] noted only eight cases of pseudomyxoma peritonaei of appendiceal origin occurring at the Mayo Clinic during the forty-year period of 1910 through 1949. In that group three patients had succumbed to the process.

SUMMARY

A case is presented in which pseudomyxoma peritonaei was noted during the course of left inguinal herniorrhaphy in 1953. The patient remained in good health in spite of the fact that at laparotomy five years later the process was still active and extensive. It was found to be of appendiceal origin. The nature of the process, its therapy and prognosis are discussed.

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DISCUSSION

Ralph H. Loe (Seattle, Wash.): About a year ago I happened to be near the operating room in which Dr. Duncan was repairing a hernia. Dr. Duncan's nurse called and said that he would like

to show me a very unusual case. What I saw was indeed a bizarre picture. The hernial sac was open and large quantities of jelly-like material resembling frog spawn were oozing out of it. The term jelly belly is aptly applied.

In the male, a ruptured mucocele of the appendix or a gelatinous carcinoma of the colon is usually the source of this jelly-like material. In the female, ovarian carcinoma may also produce this picture. In this case the La Roque incision was well used. The source of trouble was determined to be the appendix. This is the only instance of this condition that I have seen or probably will ever see again. I have seen one case of mucocele of the appendix (unruptured).

This lesion is of interest, not only because of its rarity, but because proper treatment may resolve the process despite the fact that the pathologist usually classifies the lesion as a low grade malignancy. The pathologist likes to protect himself. This lesion does not spread via the lymphatics or the blood stream. I think that it is important to re-emphasize Dr. Duncan's comments that it is worth while removing contiguous involved bowel.

Under the title of carcinoma of the appendix, twenty-nine cases of malignant mucocele were seen between 1910 and 1949 at the Mayo Clinic. There were three cases of rupture with pseudomucinous peritonaei. Two of the patients are well eight years after surgery and one eleven months after surgery. Dr. Duncan has presented a very worth while case report. This is a disease that is rare, but hopeful to the surgeon and confusing to the pathologist.

Howard C. Stearns (Portland, Ore.): I am interested in this matter of pseudomyxoma peritonaei because, like Dr. Duncan, I had one relatively recent case in a patient under my management. She came to my attention in 1954 with a preoperative diagnosis of extensive ovarian carcinoma. On opening the abdomen, this diagnosis was apparently confirmed for the abdomen was completely involved in a gelatinous, neoplastic, extensive growth. Deeply indurating growths were present on the inferior surface of the diaphragm and throughout the pelvis. The omentum was thick; the entire bowel was coated and mucous-type growth involved virtually every structure in the abdomen. Tissue was taken for study and the abdomen closed. Incidentally, the appendix seemed to be extensively involved in the same process. The following day the true picture was revealed by microscopic study to be that of pseudomyxoma peritonaei, arising possibly from the ovary or possibly from the appendix. The abdomen was reopened and the appendix and the right ovary were removed. Having read a report concerning the effectiveness of hyaluronidase on this growth I introduced 1,500 units of this substance dissolved in 200 cc. of saline solution into the abdominal cavity. A retention catheter was left in the closed abdominal wound and the following day the process was repeated. Two days later an additional 1,500 units in the same amount of saline solution was injected through the catheter which was then removed. A tremendous amount of drainage came through the wound within a day or two. It consisted of liquefied, gelatinous material. Rather marked improvement temporarily followed but the patient came back a few months later full of the same gelatinous material with the abdomen greatly distended. All possible material was scooped out and on this occasion instead of using hyaluronidase, trypsin under the trade name of Tryptar® was introduced to the extent of 250,000 units dissolved in 200 cc. of saline solution. This was repeated through a retention catheter the following day. A tremendous amount of fluid escaped from the catheter within the next two days and the abdomen receded considerably in size.

Seven months later the process was repeated because of marked abdominal enlargement. On this occasion I was amazed to find the small bowel, omental area and mesentery relatively clean of any of the pseudomyxomatous growth although there was very little diminution of the massive growths in the pelvis and on the inferior surface of the diaphragm. Trypsin to the extent of 500,000 units dissolved in 300 cc. of saline solution was introduced into the abdomen and two days later an additional 250,000 units in 200 cc. of saline solution was introduced into the abdomen through the retention catheter. This last injection, in my opinion, was a mistake for a fistula developed, and I believe that very poor distribution of the second application occurred but was probably pooled around the catheter. At any rate a reasonably normal convalescence occurred but within the last few months she has again shown marked abdominal enlargement so our therapy was palliative at best. The patient has now gone to the Mayo Clinic for whatever therapy is possible to be obtained.

I have saved as frozen material much of the solid growth and mucus for testing in the laboratory but up to the present time have not carried out any extensive studies which might indicate what enzymes would most efficiently dissolve this stuff. I hope in the future that we may light upon something of true value. At any rate, I believe that trypsin is of value and have no hesitancy in recommending it in such cases if it is properly used with caution.

Allen M. Boyden: Not infrequently one realizes that one's colleagues are shuddering over something that one does at the operating table, but it takes quite a bit for most of us to shudder over something we are doing ourselves.

About five years ago a woman who had had a pseudomucinous cyst removed ten years before in

another hospital was operated on by my associate, Dr. Shields and myself. She obviously had advanced pseudomyxoma peritonaei with partial intestinal obstruction. After the abdomen was opened we literally fought with each other to see which one could scoop out the most material into the pan on his particular side of the table.

The whole abdomen was involved. We removed the uterus and the remaining ovary and as much of this material as possible from the pelvic wall. Sheets of it were covering the intestine. The greater omentum was removed almost in its entirety. The material was not only thin but in sheets like the peel in a decortication after hemorrhage into the pleura. We concluded the operation with a Noble plication. She returned to bed in moderate shock. Her recovery was uneventful.

A few months later we did the same thing in the upper part of the abdomen, taking out the spleen, peeling the material from the liver, stomach and colon.

I have seen her recently and she is perfectly well. I mention this only to suggest that some of these patients may be relieved for long periods by what appears at the time to be a rather ghastly operative procedure.

WERNER E. ZELLER (Portland, Ore.): I have had the dubious pleasure of having one patient with pseudomyxoma peritonaei whose case I reported to the North Pacific Surgical Society about four years ago. The patient, a man in his thirties, was admitted with a loss of weight, some wasting of the extremities, and an abdomen which was getting progressively larger. We had made a preoperative diagnosis of some intra-abdominal tumor, probably carcinoma, but could not localize it by any of our x-ray findings.

At the first operation we had an experience somewhat similar to that described by Dr. Stearns. As we made the small incision in his abdomen, under considerable force and pressure a gush of fluid as well as grapelike cystic tissue rushed out. I had enough room to get my finger in and feel around, and I came against a solid mass of irregular obviously carcinomatous tissue. It was so extensive we thought nothing worthwhile could be done, so we closed the abdomen.

The next day the pathologist stated, that this was not a carcinoma but was pseudomyxoma peritonaei, so we reopened the abdomen a few days later.

I was assisted by Dr. Hinshaw. The omentum was a solid mass of this type of tissue, which was just like a bunch of grapes of varying sizes and all matted together. The peritoneum in most places was anywhere from 1 to 2 cm. thick and completely involved. We had much more than Dr. Duncan in the way of actual cyst formation. The greatest concentration of the material lay around the appendix. The omentum, and the other material we took out with it, weighed 17 pounds, and it completely filled one of the surgical wash basins.

We took out all we could find, at least all that we could get loose, and yet there was a considerable amount of material stuck everywhere.

We closed the abdomen and the patient had an uneventful recovery, returning to work almost as soon as he left the hospital. The surprising thing about this particular situation is how well the patient seemed to look and feel even though he had a tremendous amount of material in his abdomen. He did very nicely for about two years, and about the time I was getting ready to present his case before the North Pacific Surgical Society he returned with another mass in his abdomen. We repeated the process of taking out considerably more material.

He went back to work again after leaving the hospital and was actually feeling well and strong. Again his condition remained satisfactory for about two years and subsequently he came back again a third time. I did not see him on his last visit, but he has subsequently died of chronic obstruction of the bowel, ultimately an acute condition.

I had one other similar instance just last year; it was a very early situation in which during the course of cholecystectomy in an older woman I felt a little mass in the right lower quadrant around the ileocecal junction. Walled off was a little mucocele of the appendix, and some of this jelly-like material had gathered in the same area. It was no problem to take out this lower area, and she has had no subsequent trouble.

CLARENCE E. STAFFORD (Los Angeles, Calif.): I would like to apologize for presenting just one more case. This one was in a rabbit, and illustrates what happens in the experimental animal as described by Dr. Duncan in his paper.

The lesion was produced within six weeks after ligating the base of the appendix but preserving the blood supply. It displayed the typical pathological changes of pseudomyxoma peritonaei.

The microscopic appearance of this lesion was difficult to differentiate from carcinoma. A biopsy specimen was taken from the omentum of a man who had pseudomyxoma peritonaei, and this was diagnosed by the pathologist as definitely malignant. This demonstrates the complexity of trying to decide whether a lesion is really malignant or benign.

It is interesting to note that regardless of whether the lesion is diagnosed by the pathologist as being benign or malignant, the result can be lethal. In the cases which we have observed the patient may die from obstruction due to the lesion or interference with nutrition.

In regard to therapy we have been doing some work to see if it would be possible to decrease the

progress of this disease by the use of chemotherapy directed at the cellular mechanism which produces the excessive amounts of mucin. We do not have enough material to report on this, but it is another idea of a direction toward which we might direct therapy.

EUGENE J. JOERGENSON (Glendale, Calif.): I believe it was at the Yosemite meeting of our Society [1955] that Dr. Emile Holman in a discussion on wound healing in relation to stump closure gave clear evidence in favor of inversion of the appendiceal stump. In recent studies of mucocele of the appendix by Dr. Samuel Fritz of Los Angeles, it is interesting to note that there were two cases of pseudomyxoma peritonaei directly attributable to the presence of uninverted appendiceal stump, another reason for inversion of the appendiceal stump.

JOHN A. DUNCAN (closing): Dr. Loe's suggestion of inserting radioactive isotopes through a tube was considered at the time of operation. While it was not used then, it will be considered if further treatment is required.

Dr. Stearns' remarks on the use of Tryptar and hyaluronidase were most interesting, as were those of Dr. Stafford in regard to possible chemotherapy. Because of the rarity and unpredictable natural history of this condition, evaluation of such agents on a clinical basis is most difficult. Dr. Stafford's type of experimental work, somewhat similar to that of Naeslund and Cheng, may lead to a firmer foundation for therapy.

Regarding the use of the Noble plication operation as mentioned by Dr. Boyden, there would seem to be some question as to its value in pseudomyxoma peritonaei. In the far advanced case I would not expect the Noble plication procedure to delay the issue. As a measure to prevent obstructions in a case such as that presented, it would seem rather drastic.

It was remiss not to have mentioned in my paper what Dr. Zeller said about cysts. While there are very few illustrations in the literature concerning pseudomyxoma peritonaei of appendiceal origin, some have shown the formation of cysts as he mentioned. There may be many small cysts or one or more very large ones, in some instances occupying a large part of the abdominal cavity.

Dr. Joergenson's remarks concerning the relationship of mucoceles to appendiceal stumps seem important to me, particularly when the ligation and drop method is used. The objective in the use of a corrosive agent such as phenol should be not only to sterilize but also to destroy all the mucosa.

I wish to thank the discussers for their pertinent and informative remarks. They have emphasized the fact that regardless of whether this condition is termed benign or malignant by the pathologist, it certainly can be lethal. They have presented numerous valuable points on possible therapy.

Umbilical Hernia: An Inquiry into the Principle of Imbrication and a Note on the Preservation of the Umbilical Dimple

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"I'll do what Mead and Cheselden advise
To keep these limbs and preserve those eyes."
Alexander Pope

AN early interesting account of the surgical treatment of strangulated umbilical hernia appears in Cheselden's "Human Anatomy" published in 1740 [1]. This ingenious surgeon, when confronted with a strangulated umbilical hernia, resorted to the simple expedient of amputating the protruding mass of "mortified" bowel. Contrary to one's expectation, the "stoma" which resulted functioned well and in a manner compatible with health for a number of years thereafter.

Few surgeons operated upon unbilical hernias electively until the latter part of the nineteenth century. In 1898 Dr. William Mayo presented before the American Academy of Railway Surgeons a method for the radical cure of umbilical hernia. The essentials of this method were (1) wide excision of the umbilicus and surrounding skin and (2) imbrication of the aponeurotic structures and peritoneum in a transverse direction. Imbrication was accomplished with a large curved needle and stout linen sutures threaded through the upper flap from without at a distance from 2 to 3 inches above the margin of the opening.

This method was described again before the American Surgical Association in 1901, a third time before the American Medical Association in 1903, and the ultimate results in 126 hernias were then reported in the *Journal of the American Medical Association* in June, 1907 [2]. Mayo stated that "Although the operation frequently fails, the relapse is less uncomfortable to the patient and has less danger of strangulation than the original hernia . . . the return partakes more of the nature of a ventral hernia, the internal opening being nearly if not quite the diameter of the protrusion."

The principle of imbrication of fascial aponeuroses was later adapted by a number of surgeons in the repair of other aponeurotic defects such as those found in inguinal and diaphragmatic hernias. A search of the available literature failed to disclose scientific evidence to support the view that imbrication of fascial aponeurotic structures offers increased tensile strength over simple apposition of freshly cut surfaces. It is a common observation, for example, that the inadvertent overlapping of skin edges in the suture of an ordinary wound may actually result in decreased tensile strength.

Prior to the "imbrication era" surgical attempts at repair of umbilical hernia involved extensive dissection of the rectus muscles with an attempt to unite them vertically in the midline. The results were "so unpromising" that few surgeons cared to attack them. It is significant that the improvement of results in this operation accompanied not only the introduction of the principle of imbrication but also perhaps more importantly the closure of the aponeurotic defect in a *transverse* direction. Inasmuch as the fibers of the external and internal oblique and transversus abdominis aponeuroses are running in a transverse direction in the components of the rectus sheath, a transverse closure results in a line of suture at

right angles to the direction of the fibers. Such a suture line receives less tension during increases and decreases in the anteroposterior diameter of the abdomen accompanying respiratory movements. (Fig. 1.)

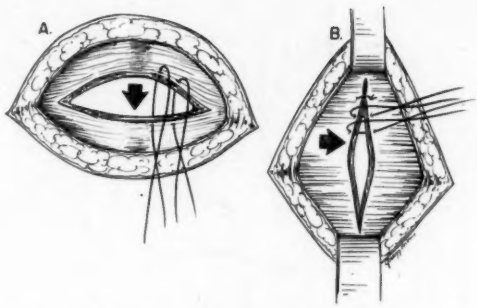

FIG. 1. A, closure in transverse (anatomic) direction. B, vertical closure (wrong) with sutures parallel to direction of fibers.

EXPERIMENTAL OBSERVATIONS

With these considerations in mind and with a conviction that imbrication of the aponeuroses was of lesser importance than closure in a transverse direction, a series of experiments was carried out. A group of rabbits of comparable nutrition and age and in good health were operated upon under sterile operating room conditions.

Following surgical preparation of the abdomen, a transverse incision was made at the level of the umbilicus and a defect created in the anterior abdominal wall through all layers simulating an umbilical hernia. The transverse incision averaged 6 cm. and a circular defect in the mid-portion (analogous to an umbilical hernial defect) measured approximately 1 cm. in diameter.

In half these animals the defect was repaired by the imbrication method, overlapping from above downward and utilizing interrupted sutures of No. 32 stainless steel wire.

In the other half the defect was closed by interrupted sutures of the same material with simple apposition of the freshly cut surfaces. (Fig. 2.)

Prophylactic penicillin was given and animals which became infected were discarded from the experiment.

Seven days later an intraperitoneal balloon was introduced through a tiny stab wound into the abdomen and secured so as to be airtight. With the animal under anesthesia, the skin incision was carefully opened and the stainless steel wire sutures were removed. The balloon was inflated with oxygen at a constant rate utilizing a flow meter. The bursting strength of the wound (apart from the sutures) was

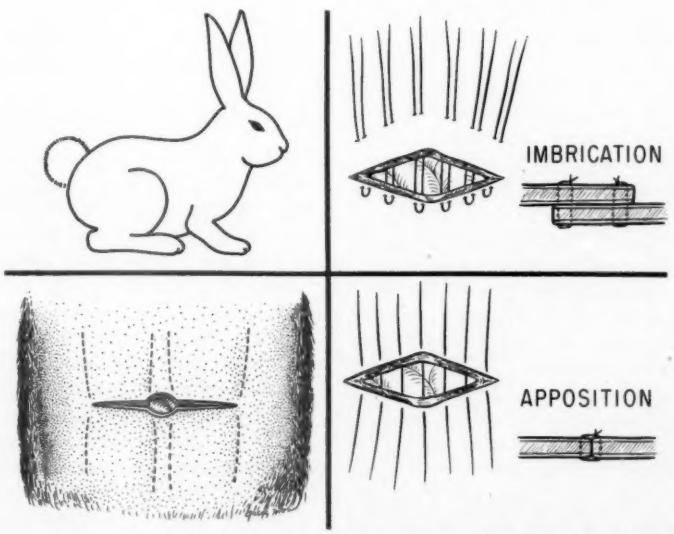

FIG. 2. Experiments simulating umbilical hernia. Closure by imbrication and simple apposition.

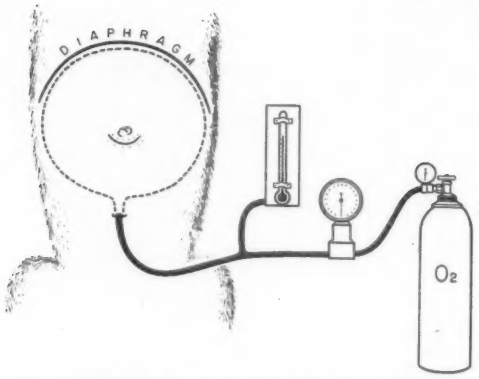

FIG. 3. Inflatable intraperitoneal balloon attached to the source of O_2, and to a flow meter and manometer to measure bursting strength of experimental wound.

recorded by an attached mercury manometer. (Fig. 3.)

At the completion of this experiment in several animals the wounds were resutured with simple through and through opposing interrupted No 32 stainless steel wire sutures, and the bursting strength again measured at the end of a second seven-day period.*

Results. Table 1 lists some representative results. The average bursting strength in the two methods was not significantly or statistically remarkable. However, two of the lowest bursting strengths, viz., 44 mm. Hg and 30 mm. Hg, occurred in the closures which had been imbricated. It became apparent in other experiments that the bursting strength of the wound could be impaired almost proportional to the amount of overlapping. The resulting increased tension accompanying excessive overlapping not only impaired healing but also compromised the vascular supply to the operative site.

It appears, therefore, that in rabbits, experiments designed to measure the force necessary to produce rupture of a transverse wound indicate that one seven days old will regularly rupture at levels between 60 and 70 mm. Hg as measured by the inflatable interperitoneal balloon. Imbrication of fascia in this experiment does not result in increased tensile strength and, as a matter of fact, if carried to extreme may impair it.

* Many of these experiments were conducted with the kind help and collaboration of Dr. Harry Davis. It is planned to pursue this study further and report the results elsewhere.

TABLE 1
RESULTS OF EXPERIMENTS

Experiment No.	Imbrication (Bursting Strength at 7 Days)	Apposition (Bursting Strength at 7 Days)	Secondary Apposition (Bursting Strength at 14 Days)
1	44 mm. Hg	78 mm. Hg	.....
2	83 mm. Hg	70 mm. Hg	.....
3	60 mm. Hg	55 mm. Hg	170 mm. Hg
4	100 mm. Hg	75 mm. Hg	.....
5	74 mm. Hg	54 mm. Hg	160 mm. Hg
6	30 mm. Hg	61 mm. Hg	180 mm. Hg
7	70 mm. Hg	84 mm. Hg	300 mm. Hg
Average....	65 mm. Hg	68 mm. Hg	.....

However, if the bursted wound is simply resutured by the through and through technic and seven more days are allowed to elapse, the pressures necessary to produce rupture of the wound are in the neighborhood of 170 mm. Hg. (In one animal disruption required 300 mm. Hg.) This observation has been made by others. It not only suggests that there is no "lag" at the time of the secondary suture but also accounts for the interesting fact that wound disruption rarely occurs in the same individual a second time. It also suggests that tissue extracts of traumatic wounds appropriately prepared and injected into an operative site prior to a primary operation might achieve a similar accelerated rate of healing.

CLINICAL OBSERVATIONS AND TECHNIC

The original descriptions of operations for umbilical hernia invariably include wide excision of the umbilical dimple. In addition, several modern textbooks and articles as recent as 1956 imply that this maneuver is an important part of the operation.

For more than ten years we have believed that excision of the umbilicus is not only unnecessary but also may produce undesirable psychologic results, particularly in children and esthetic adults. Profound inferiority patterns and psychopathic behavior problems in children have been attributed to the excision of the umbilical dimple. Preservation of what at first thought might appear to be an insignificant part of the human anatomy may be of importance in the integrated development of the

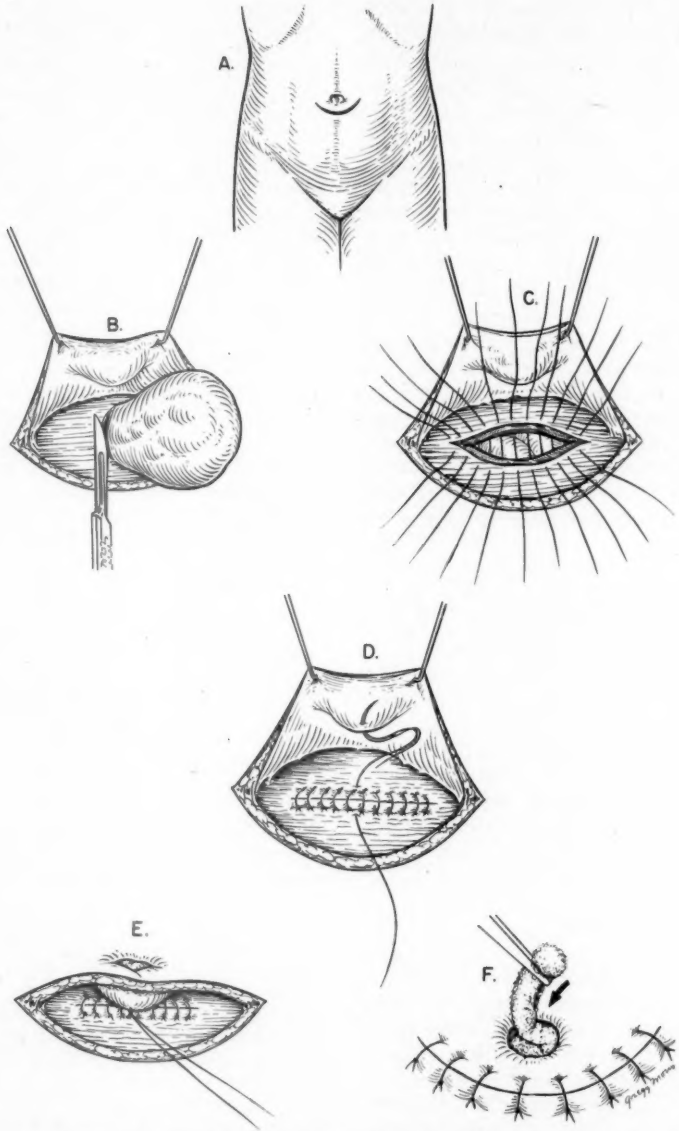

FIG. 4. Technic of repair of unbilical hernia illustrating through and through simple apposition and preservation of the umbilical dimple. A, skin incision. B, excision of properitoneal fat and sac. C, fascial sutures. D and E, anchoring stitich to preserve umbilical dimple. F, stent (cotton).

adjusted adult personality. Furthermore, it is a refinement in the operation which no thoughtful surgeon upon reflection would willingly omit. Thirty-nine patients have been operated upon in this manner. There were thirty-five females and four males; the youngest patient was six years of age, the oldest eighty-three. In all instances a satisfactory umbilical dimple has been preserved and there are no known recurrences.

The majority of these hernias occur in somewhat obese females with flaccid abdominal walls, and repair may be accomplished quite simply when done electively. An elliptic incision with the concavity directed downward is made at the inferior aspect of the umbilicus. (Fig. 4.) The skin flaps are reflected upward and downward, exposing the aponeurotic fasciae overlying the rectus muscle and surrounding the hernial defect. The hernial protrusion which invariably includes properitoneal fat and peritoneum and omentum is amputated. The omentum is returned to the peritoneal cavity and no effort is made to close the neck of the sac as a separate structure. The defect is enlarged in a transverse direction and the edges freshened by excision. Closure is then accomplished by simple apposition, utilizing fine sutures of non-absorbable material in a through and through manner. This single-layer closure secures all components of the aponeurotic fascial layers as well as the peritoneum.

A single fine suture is then placed so as to unite the external fascial surface to the apex of the undersurface of the umbilical skin. The skin is closed with fine interrupted sutures, and a moist cotton stent is placed in the umbilical recess and held in place by a small pressure dressing.

Adults rarely require more than forty-eight hours of hospitalization. A number of these procedures were performed on the day following delivery in postpartum patients without extending their normal convalescence.

COMMENTS

From these observations, both experimental and clinical, it would appear that the principle of imbrication offers little or no advantage over simple apposition of aponeurotic fasciae. This is particularly true when applied to the repair of an umbilical hernia. Furthermore, whether this principle offers advantages in the repair of other aponeurotic defects is open to question.

Although operation is rarely indicated in infants and young children, it is of importance to advise repair in all adults. There is a high potential for incarceration and strangulation with an accompanying significant mortality. The physician who fails to advise repair of an umbilical defect assumes a grave responsibility for the future welfare of his patient. Because the defects are usually small, protrusion of bowel, when it does occur, may be rendered irreducible by minimal inflammatory changes. Preservation of the umbilical dimple is an important refinement in the operation.

Acknowledgment: We are indebted to Dr. Harry Davis for his valuable suggestions and particularly for his help in devising the apparatus for measurement of the bursting strength of wounds. We also gratefully acknowledge the medical library of Dr. Robert J. Moes as an original source of bibliographic data used in this paper.

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DISCUSSION

Clarence J. Berne (Los Angeles, Calif.): In any discussion of this excellent paper one can, I think, assume that transverse closure of the hernial defect is desirable. The basic question raised concerns the relative worth of edge-to-edge approximation of the fascial edges and the method of fascial overlapping. The fundamental question is therefore whether or not the healing process is more effective when the cut surfaces are approximated edge-to-edge. Other inherent variables are the amount of tension on the sutures, the type of suturing and the surface area of the approximated tissues. These are interrelated and not separate variables. Tension from too much overlap could easily vitiate any benefit from overlap if, in fact, it is actually desirable.

It is worth noting that the rate of fascial healing is depicted in a recent surgical textbook. About 80 per cent of the ultimate tensile strength is attained in approximately twenty days. This is a commonly held concept. Recent studies by Douglas have shown that approximately 200 days are required, rather than the previous figure. Part of this difference may lie in the field of methodology. However, it does present the problem of deciding on the optimum time for determining the degree of fascial healing. Also, is is possible that in the present problem distention of the peritoneal cavity with air injected through a needle, or the use of an inflated balloon, or direct measurement of fascial healing with a Sandblom tensiometer might not give comparable results.

In considering the technic of the overlap operation there are several factors worthy of discussion.

A recent monograph on the surgical treatment of hernia recommends that for umbilical hernia in the adult, all the subcutaneous fat should be cleaned off the subcutaneous surface of both flaps. I think one can question the value of uselessly denuding the upper flap fascia of its tela aponeurotica. This devascularizes it and adds to the dead space of the wound. The recommendation is also made that the peritoneum be left on the underside of the upper flap. This constitutes interposition, similar to that of muscle in fractures. This advice should be seriously questioned. Another technical detail of the overlap procedure has to do with the mattress tension sutures, especially the number of them and the tension with which they are tied. Unwisely placed, they can isolate the circulation of the upper flap and actually convert the operation into a grafting procedure. Because the linea alba is what Ogilvie terms a "felt" tissue, the midline mattress suture can be transversely placed. However, if the lateral sutures are placed as vertical mattress sutures, they not only are then at a right angle to the fascial fibers but also probably encroach much less on the blood supply. Both features seem desirable.

I would like to summarize a recent report on umbilical hernia made by Gibson and Gasper from the Los Angeles County Hospital. Their study consisted of approximately 100 cases, with a one- to nine-year follow-up. About half the cases had been treated by edge-to-edge approximation and the others by the classic "vest over pants" overlapping procedure. There was approximately an 8 per cent recurrence rate in both groups. The overlap procedure was used for the larger hernias. In this series emergency surgery for complications of umbilical hernia was associated with a mortality rate of 10 per cent. This latter figure should furnish an adequate basis for a strong negativistic attitude by all surgeons toward any dilatory advice regarding elective surgery for umbilical hernia.

I want to congratulate Dr. Farris and his coworkers for their presentation on this often slighted subject. Ambroïse Paré's "punctus aureum" for inguinal hernia fell by the wayside after four centuries, and further study may do the same for our traditional method of management of umbilical hernia.

Dr. J. Englebert Dunphy (Boston, Mass.): I am sorry that the statistics in the authors' experiments show so little advantage for an approximation over an overlap; on the basis of current information an approximation should be substantially better. This is an experiment I would like to repeat, and I think when the overlap is excessive there may be factors other than tension involved.

I would agree completely with Dr. Berne's comment about the importance of fat. Fascia heals by connective tissue repair. Where do the cells come from that supply this? They do not come from fascia. The fascial cells themselves take no part in the repair, at least in the early phases. The origin of the connective tissue cells is not known for certain, but there are good reasons for believing that it is the loose areolar tissue or adjacent fat. Therefore, when you strip the fat widely off fascia and particularly if you overlap it, you literally isolate it from the sources of new cells that are going to bring about the repair.

The interesting studies of Douglas to which Dr. Berne referred fit very well with this concept. The early phase of repair studied by Howes and Harvey, the ten- to fourteen-day repair, is due to connective tissue just like any other healing wound, and the long, steady, late gain which may be variable under different circumstances is due to a gradual change of the connective tissue cell into a fascial-like cell or actual replacement of the connective tissue by a fascial cell. Which is the case is not known, but in either event you can see that with the overlap and the deprivation of a source of supply for good connective tissue, you theoretically at least impair the initial tensile strength and even the late gain may be prolonged.

The studies of Allen and Mason on tendon repair also showed that there are two phases to repair: the early phase in which rest and non-use of the tendon is important (the connective tissue phase) and the late phase which is favored by activity and a certain amount of use and tension (the stage of cellular transition).

David Metheny (Seattle, Wash.): In 1943 I operated upon a patient with a recurrent inguinal hernia that had been repaired by Sir Frederick T. Reeves in 1903, forty years previously; he had overlapped the fascia. The recurrence was not an indirect hernia, which he had repaired, but a new direct hernia, and it was interesting to see the overlapped fascia after forty years had elapsed. It was adherent at each edge, that is, where each edge had been tacked down. In between there was no adherence at all. If you can make anything of that, do so.

Edward N. Snyder, Jr. (Pasadena, Calif.): Some years ago I became enthusiastic about the transverse repair of umbilical hernias with direct apposition of the fascia. When I read that this article was going to be presented, I reviewed all the umbilical herniorrhaphies that had been performed at the Huntington Memorial and St. Luke Hospitals in Pasadena between January, 1946 and January, 1956. I was hoping, of course, to show (just as Dr. Dunphy said) that those men who had not used Dr. Farris' technic were going to have a lot of recurrences.

Basically eight technics of umbilical herniorrhaphy were used: transverse repair with direct apposition of the fascia; transverse repair with imbrication; vertical repair with direct apposition;

vertical repair with imbrication. In any of these the umbilicus can be saved or excised. Although the umbilicus was preserved in 157 of the 224 cases, the actual technic of fascial repair was quite varied, with the majority of cases being repaired transversely with imbrication. Only forty-four defects were repaired in the manner presented by Dr. Farris and his co-workers.

The facts of greatest interest to me are: First, only two of the 224 patients had had umbilical herniorrhaphies prior to January, 1946. Second, I have been able to find only one postoperative recurrence since January, 1956. This was in a patient who had not undergone previous herniorrhaphy. I hate to say this, but the defect had been repaired with the technic the authors described.

JACK M. FARRIS (closing): I am grateful to Dr. Berne for his thoughtful and pertinent remarks. Also, it was a pleasure to have the paper discussed by such an eminent authority as Dr. Dunphy.

One might resolve this issue by stating that there is no evidence to support the view that imbrication is any better than apposition. It does seem reasonable, however, that if one imbricates tissue excessively enough he is going to compromise its blood supply. A series of mattress sutures placed 3 inches above the superior cut surface and tied under tension is simply an ingenious way of applying a tourniquet to the wound.

I would like to thank Dr. Metheny and Dr. Snyder for their most appropriate remarks. It may be worth pointing out that in Dr. Snyder's group of patients it is quite possible that apposition was only used in those in whom closure of the defect was accomplished with difficulty in the presence of increased abdominal tension.

Carcinoid Tumors of the Rectum

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DURING the past twelve years considerable interest in carcinoid tumors of the rectum has been observed, as evidenced by the greater number of reported cases and the increasing tendency to emphasize the malignancy of this tumor.

We recently observed a large carcinoid of the rectum in a ten year old boy and believe that a clinical and pathological review of carcinoid tumors of the rectum, as well as a report of such a case occurring in the youngest patient encountered in the medical literature, might prove to be of interest.

Lubarch reported the first two cases of carcinoid tumors of the ileum in 1888, and in 1907 Obendorfer stressed the benign nature of these lesions. However, the emphasis within recent years has been rather on the malignant potential of carcinoid tumors.

Saltikow reported the first rectal carcinoid in 1912, and Brunschwig reported the second such case in 1933. Only four more cases were reported by 1942. Raven noted that approximately sixty cases were reported by 1950, and there are approximately 150 reported surgical and autopsy cases in the literature at the present time. The youngest patient was a fourteen year old boy reported on by Feyrter in 1934, in whom a carcinoid of the rectum was discovered as an incidental finding at autopsy. This sudden increase in the incidence of carcinoid tumors of the rectum is due not only to the increased use of the sigmoidoscope but also to the increased awareness of the existence of this lesion on the part of both the surgeon and the pathologist.

Until recently it has been stated that the majority of carcinoid tumors were found in the appendix. Foreman stated that 85 to 96 per cent of carcinoid tumors were found in the vicinity of the ileocecal valve. However, more recently (1954) Jackman found that in a seven-year period from 1947 through 1953, 112 carcinoid tumors were encountered at the Mayo Clinic, and forty-four (39.3 per cent) involved the rectum. Interestingly enough, there were only two instances of carcinoid tumors involving the appendix in this series. Thus, any figures showing the relationship of the incidence of carcinoids of the rectum to carcinoids elsewhere in the body would seem to be quite variable.

Except for occasional rectal bleeding due to superficial mucosal ulceration, rectal carcinoids are relatively asymptomatic and are usually discovered during rectal or sigmoidoscopic examination.

The variation in the malignant nature of carcinoids may well be related to their location, lack of symptomatology and the difficulty in making a diagnosis. For instance, carcinoids of the appendix very rarely metastasize, as the appendiceal lesions are small and are removed either during a routine appendectomy or when the carcinoid tumor causes an obstructive type of appendicitis. However, it has been estimated that 10 to 12 per cent of rectal carcinoid tumors metastasize. These tumors become larger than the appendiceal carcinoids but still are quite readily found at the time of rectal or sigmoidoscopic examination. On the contrary, about 35 per cent of the carcinoids of the ileum metastasize as no symptoms are produced until the tumors become large enough to obstruct the lumen of the bowel.

Grossly, the extra-appendiceal carcinoids are firm yellow or gray submucosal nodules and frequently are accompanied by a fibrous tissue hyperplasia, resulting on occasions in fibrous annular constriction of the intestine. The mucosa overlying the tumor is nearly always intact; however, the carcinoid may invade into and through the muscular and serosal layers of

the bowel. At times the carcinoid may invade adjacent mesentery, causing the formation of large masses of fibrous tissue which may be several times the size of the primary carcinoid tumor and be wrongly diagnosed at the time of surgical exploration as huge metastatic lymph nodes.

The microscopic picture of the nests or columns of small uniform round polygonal epithelial cells lying in a fibrous stroma is quite diagnostic of a carcinoid tumor. Frequently, such tumors in the appendix and small intestine display the property of argentaffinity; however, this is rarely noted in rectal carcinoids. Gasset and Masson in 1914 first demonstrated this property of certain carcinoid tumors and showed that the intracytoplasmic granules stained black with silver stain. The fact that the Kultschitzky cells situated in small numbers in the bases of the crypts of Lieberkühn contain identical argentaffin granules has given rise to the belief that carcinoid tumors may arise from such cells. However, this would not account for the large number of carcinoids which fail to display any argentaffinity. Foreman has emphasized the fact that the normal beta cells of the pancreas readily take up the silver stain, and thus he believes that the term argentaffin tumor should not be generally employed for carcinoid tumors.

Erlanger has shown that the chemical enteramine is the substance in the granules which causes them to become blackened by ammoniacal silver nitrate. Interestingly enough, the typical symptoms dominating the clinical picture of abdominal carcinoid are a result of the increased secretion of 5 hydroxytryptamine (serotonin) from excessive amounts of the tumor tissue which, when examined with the silver stain, shows this argentaffinity.

The chemical serotonin is a naturally occurring amine in the blood stream in small amounts known to have a potent effect on all smooth muscle. Page believes it is also the vasoconstricting substance present in traumatized serum. He believes it may develop from the blood platelets as well as from argentaffin cells. The fascinating clinical syndrome associated as a rule with metastasis to the liver from carcinoid tumors may readily be explained on the basis of elevated blood serotonin levels. The presence of excessive amounts of serotonin in the blood produces a flushing of the skin with cyanosis due to the pronounced contraction of the arteries and arterioles, accompanied by dilatation of the capillaries and venules. The contraction of the smooth muscle in the pulmonary circulation results in greatly elevated pressure in the pulmonary artery and right ventricle, with subsequent valvular deformity and endocardial fibrosis. Similarly, the contraction of smooth muscle results in bronchoconstriction and the intestinal cramping so frequently present. The pellagra-like changes which are seen are due to the decreased amount of niacin being formed from tryptophan as a result of the tremendous amount of serotonin being formed instead from the amino acid tryptophan.

Pernow examined thirty-three patients with carcinoid tumors. All who had the symptoms just discussed had high serotonin levels and carcinoid tumors with metastasis to the liver, except one patient who was found to have a non-malignant ovarian teratoma with large numbers of argentaffin cells. Following surgical removal of the ovarian tumor, all the clinical symptoms disappeared except the cardiac changes, and the serotonin studies returned to normal.

CASE REPORTS

Two patients with proved carcinoid tumors of the rectum, and one probable case, have been seen at The Samuel Merritt Hospital in Oakland, California. One patient is the ten year old boy mentioned previously; the other two patients had extensive metastasis to the liver when operated upon a few months ago.

The first patient was operated upon in 1934 at the age of thirty-three. A small rectal tumor was locally removed from below and was diagnosed as a grade IV adenocarcinoma. Radon seeds were subsequently applied and the patient was given x-ray therapy. He was in excellent health until 1952, when recurring attacks of chills and fever developed, increasing in frequency. Extensive metastasis to the liver from a carcinoid lesion was proved at operation in April, 1958, and at autopsy examination five months later. At this time the liver weighed over 8,000 gm., being nearly completely replaced with tumor tissue typical of carcinoid. Because this tissue did not take the silver stain and there was no definite evidence of a primary lesion, it seemed most likely that the primary lesion had been a rectal carcinoid which had been erroneously diagnosed in 1934 as a grade IV rectal carcinoma. Small cell carcinomas of the rectum have been mistaken structurally for carcinoids, as noted by Pearson and others

The second patient underwent local excision for a rectal carcinoid in 1949 at the age of forty-seven. He was well until October, 1957, when attacks of chills and fever first developed, increasing in frequency and accompanied by anorexia and fullness in the right upper quadrant. On March 6, 1958, abdominal exploration showed that the liver was filled with numerous nodules 2 to 3 cm. in size. Microscopic section revealed typical carcinoid tumor which was identical with sections of the rectal carcinoid which had been removed in 1949. The tissue failed to take the silver stain. Interestingly enough, this patient received a course of cobalt therapy postoperatively and is in excellent health at the present time.

The third case is that of a ten year old boy whom I was asked to see on January 27, 1958. This patient had noted slight rectal bleeding for two weeks, and when examined by his physician a large mass was found in the region of the prostate. He was referred to a urologist, Dr. James L. MacDonald, who noted that a cystogram was normal except for the presence of calcium in the mass.

Rectal examination revealed a hard, fixed, nontender mass approximately 7 by 3 cm. in the region of the prostate, involving the anterior rectal wall. This mass could also be palpated through the perineum, extending up toward the posterior urethra. The remainder of the examination, laboratory work and x-ray film of the chest were entirely normal. Dr. MacDonald and the senior author discussed frankly the diagnostic and surgical possibilities with the boy and his parents, and the following day, with the patient under general anesthesia, sigmoidoscopic examination was performed. The mass extended to .5 cm. of the anal margin, and a good-sized biopsy specimen of the tumor was taken through the anterior rectal wall. Frozen section examination revealed probable carcinoid tumor of the rectum. Because of the large size and fixation of the lesion, one-stage combined abdominoperineal resection was performed, freeing up the bladder and dissecting the mass off the posterior urethra and bladder neck. The patient's postoperative course was entirely satisfactory, and at present he is actively engaged in athletics and is a brilliant student. Further pathological study revealed that strands and cords of cells typical of carcinoid tumor extended out through the muscle coats of the bowel and beneath squamous epithelium of the anus. Silver stain studies made on the tumor tissue were entirely negative.

Incidentally, serotonin studies were made several times on all three of these patients, and never showed the presence of an increased amount. The evidence of metastasis, proved in one case and most probable in the other, as well as the extensive nature of the primary lesion in the ten year old boy, makes one hesitant in considering local excision of such lesions.

In considering the surgical treatment of rectal carcinoids, we would most certainly agree with Pearson and Foyle who state that they believe "all carcinoid tumors are malignant and that all will manifest malignancy if permitted to fulfill their natural course." With this thought in mind, we would definitely agree with the conclusions of Shepard and his co-workers and others who believe that a single nodule 1 cm. or less in diameter might be locally excised with careful follow-up examinations. However, radical resection of the lower rectum for lesions over 1 cm. in size, or any lesions which are ulcerated, fixed or infiltrated, is recommended.

SUMMARY

1. A comparison of the incidence, symptoms and pathology of rectal carcinoids with those elsewhere in the intestinal tract is given.

2. Although rectal carcinoids and their metastasis have the same microscopic pattern as other carcinoid tumors, the lack of argentaffinity is noted.

3. The effects of increased blood levels of serotonin are discussed.

4. Three cases of rectal carcinoids are presented, one proved, one probable with extensive metastasis to the liver, and the other in a ten year old boy with a large primary rectal tumor. None revealed any elevation in the serotonin levels.

5. Radical resection of the rectum is urged for patients who have rectal carcinoids over 1 cm. in size or for any carcinoid tumors revealing ulceration, fixation or infiltration of the rectal wall.

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DISCUSSION

ROBERT A. SCARBOROUGH (San Francisco, Calif.): I share the authors' healthy respect for the malignant potential of carcinoid tumors of the rectum. They have presented additional evidence that these tumors are not infrequently malignant, do metastasize and may kill.

In the past eight years I have had ten patients with carcinoid tumors of the rectum. In seven of these ten patients a firm submucosal lump, entirely asymptomatic, was an unexpected finding on digital palpation of the rectum in the course of a physical examination; yet three of these seven patients had metastases to intra-abdominal regional nodes. In two of the three, the primary lesion was not over 1 cm. in diameter, and was not ulcerated, fixed or grossly infiltrating.

The true nature of these lesions is frequently unsuspected until microscopic examination is made. Even then the pathologist cannot tell us whether or not a carcinoid is malignant and liable to metastasize. This is in sharp contrast to the pathologist's ability to differentiate a benign adenoma and a malignant adenocarcinoma. Furthermore, it is not an uncommon error to call a carcinoid a poorly differentiated adenocarcinoma. This apparently occurred in oue of the authors' reported cases. Three of my own ten patients were referred with a mistaken microscopic diagnosis of adenocarcinoma.

The record of treatment in these ten patients may well confuse rather than clarify the issue of the proper procedure to use in the treatment of carcinoid tumors of the rectum. It is a record of my own confusion and concern about this real problem.

In four of the ten patients local excision has been the only treatment. These patients have remained well from one to eight years, but I am not at all sure they will remain well. The authors have reported just one instance of fatal metastases to the liver twenty-four years after treatment of a primary rectal tumor. Other such examples have been reported.

A fifth patient in my group is also an example of slow progression of disease. A twenty-one year old man with a proved primary carcinoid of the rectum underwent abdominal exploration in 1952 and was found to have a huge inoperable pelvic tumor and many large metastatic mesenteric nodes. When last examined eight months ago the large pelvic and rectal tumors were apparently unchanged and the patient felt quite well.

In a sixth patient abdominoperineal resection was performed because of an entirely separate adenocarcinoma of the rectum. It was this patient's good fortune to have neither adenocarcinomatous or carcinoid metastases to the regional nodes. This case demonstrated another interesting facet of the problem of carcinoids, namely, the not infrequent simultaneous presence of an adenomatous neoplasm. This was so in four of these ten patients.

In the final four patients radical resection has been performed: three abdominoperineal resections and one segmental resection with re-anastomosis. All three patients undergoing abdominoperineal resection had a metastatic carcinoid in multiple regional nodes. I am chagrined to say that the pathologist responsible for the examination of the surgical specimen removed by segmental resection did not bother to look for or section any regional nodes.

I would like to point out that the appropriate selection of these four patients for radical resection was entirely fortuitous and was not made on the basis of any personal insight which could have determined which of these ten patients had metastases and therefore should undergo radical resection.

One of these four patients was explored because of the additional finding of a sigmoid polyp. A number of hard regional nodes up to 2 cm. in diameter were found and proved to be metastatic carcinoid by frozen section. It is now more than three years since abdominoperineal resection was performed and there is no suspicion of recurrent disease.

Another patient, referred two months after local excision of a 1 cm. carcinoid, had an apparent local recurrence beneath the healed scar. Abdominal exploration revealed several large regional nodes filled with metastatic carcinoid. Abdominoperineal resection was performed four years ago. She has recently had a baby and appears perfectly well.

The third patient had a grossly ulcerated and infiltrative primary carcinoid measuring 4.5 cm. in diameter. The specimen removed by abdomino-

perineal resection contained evidence of metastases to multiple regional nodes. This patient died of disseminated metastases two years later.

The fourth patient had segmental resection for a carcinoid of the upper rectum and two adenomatous polyps of the distal sigmoid. This patient showed no suspicion of recurrent disease after four years, but was then lost to follow-up.

In conclusion, I would like to endorse the authors' recommendation of radical resection for any rectal carcinoid over 1 cm. in size, or revealing ulceration or infiltration.

I also agree, but with less conviction, that small discrete submucosal lesions may be locally excised with careful follow-up examination. It should be pointed out, however, that such examination is of value only for evidence of local recurrence and fails to detect the possible presence of metastasis to regional nodes. I am inclined to believe that it would be advisable to perform abdominal exploration two or three months after local excision, with a careful search for any evidence of metastases to regional nodes. If this were found, certainly radical resection would be indicated.

DAVID METHENY (Seattle Wash.): I want to thank both the authors and Dr. Scarborough for bringing out something I had not realized so much before, that this lesion is really under the submucosa; one thinks of these lesions as presenting themselves.

I would like to comment on a rather advanced case of carcinoid I saw; I do not know if it was located in the rectum. At a cancer meeting in Seattle some years ago, a visiting doctor came and sat beside me. I did not know him very well, but as the lecturer was talking about cancer my attention was drawn to the man beside me because of the intestinal roar and growling he had. I confess my mind wandered from the lecturer as I contemplated what was going on.

It seemed to me it could not be a peristaltic rush, at least uncontrolled, so I took a glance at the man from the side and noticed that his face was flushed. At the time I thought it was embarrassment, but since it continued during the course of the lecture I thought he must be having some kind of intestinal obstruction or some cramping so I watched to see if there was evidence of pain on his face. He apparently was not in pain. After the lecture was over I saw him talking to a good friend of mine. Later I went to my friend and asked him if he knew this doctor. He said he did. I told him I thought the man should see someone and find out what was happening. My friend told me he had operated upon the man and had found inoperable carcinoids throughout his body.

Of course, all these symptoms were from the serotonin. I think sometimes we slip up on these conditions when we do not think of them.

GROSVENOR T. ROOT (closing): Dr. Scarborough mentioned the increased incidence of primary carcinoma in patients who have carcinoid tumors. As noted in the literature, in about 8 per cent of patients who have a primary carcinoma another primary tumor will develop elsewhere in the body; however, in 40 to 60 per cent of patients who have carcinoid tumors other primary carcinomas have been noted to develop.

Hirschsprung's Disease with Extensive Aganglionic Segments

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MUCH has been written about Hirschsprung's disease in the decade since Swenson's classic work [1–3]. However, when we recently encountered several patients with extensive aganglionic segments, we found such a paucity of information on this particular problem that we believed it would be worthwhile to record the experience with four such patients seen at Children's Hospital of the East Bay in the past four years: one patient in whom the entire colon was aganglionic [4], and three others having almost identical lesions in whom the aganglionic segment extended to the splenic flexure.

Early diagnosis and treatment in these cases is essential for survival. In the usual case of Hirschsprung's disease with only short segments of rectum and sigmoid involved, the child will usually get along on medical management for several to many years before coming to operation. In the cases herein described in which a long segment of the terminal bowel acts as an obstructing element, complications develop early.

FIG. 1. The baby's abdomen becomes distended and loops of bowel with peristaltic waves can be seen through the abdominal wall.

The clinical picture is that of partial intestinal obstruction. The usual picture of this disease presents as having obstipation early but our patients had fairly frequent small, soft to watery stools two to thirteen times a day. However, in spite of this obvious patency of the intestinal tract, the babies vomit bile-stained material repeatedly and become markedly distended. (Fig. 1.) Depending on the stage in which seen, the abdomen is soft or increasingly tight. No masses are palpable but the pattern of distended bowel may be seen through the thin abdominal wall. Peristalsis is present and varies from time to time from hypo- to hyperactive. Rectal examination reveals a collapsed rectum which is either empty or contains only a small amount of stool. The patients may be given adequate fluids but their condition deteriorates progressively. The picture, thus, is that of partial intestinal obstruction and may be simulated by other lesions such as duodenal diaphragm or atresias along the gastrointestinal tract.

A scout film of the abdomen usually confirms this impression, although in retrospect, an x-ray film taken at this stage could have given us the diagnosis. With such a roentogram a barium enema should be the next step. Two things are characteristic. The first is the demonstration of transition from a narrow to a dilated segment of bowel (Fig. 2), and the second and equally helpful sign is the evidence of retention of the contrast media in the bowel as shown by a roentgenogram of the abdomen taken twenty-four hours later. (Fig. 3.)

FIG. 2. The transition from a distended transverse colon to a smaller descending colon occurred at the splenic flexure in three cases, but was overlooked when first encountered.

Swenson suggests confirmation by rectal biopsy at this stage, and such would have been useful had it been thought of in the patient with completely aganglionic colon. However. it is generally unnecessary as these findings, with the baby's clinical picture, should be sufficient to make a definitive diagnosis.

CASE REPORTS

CASE 1. S. B., a full term male infant who weighed 8 pounds, 14 ounces at birth (normal delivery), was first admitted to Children's Hospital of the East Bay on July 25, 1954, at the age of eight days because of vomiting during the past twenty-four hours. The vomitus was at first greenish, it then became yellow, and the patient was unable to retain any feedings. There was no recent change in his stools which had always been rather watery and which he passed several times a day.

The family history disclosed that one sibling had had an operation for an intussusception at nine months of age.

Physical examination showed a well developed, slightly dehydrated baby who was otherwise normal.

During the examination he passed a watery, foul-smelling, greenish stool; during the next twenty-four hours he had twelve more bowel movements. The patient was given antibiotics and intravenous fluids and there was a prompt improvement in his condition. He was started on a different formula and his bowel movements decreased to two a day. He was discharged on the fifth day.

FIG. 3. Contrast media remaining in the colon twenty-four hours after a barium enema.

The baby was readmitted four days later with diarrhea and vomiting. He again responded promptly to the administration of parenteral fluids and was discharged on the ninth day with the diagnosis of gastrointestinal allergy due to cow's milk. Stool cultures on both occasions showed no pathogenic organisms.

His final admission to Children's Hospital was at the age of seven weeks. At that time he weighed 9 pounds, 9 ounces. He had had recurrent diarrhea and intermittent vomiting during the interval. His physical examination showed moderate abdominal distention, dehydration, and some wasting. A check of his duodenal drainage showed trypsin activity. Examination by barium enema on September 17, 1954, was reported "unsuccessful because of the fact that the colon was filled with fecal matter." Considerable air was noted in the small intestine. Excretory urograms showed no abnormality in the urinary tract. A repeat barium enema showed no intrinsic lesion or obstruction of the colon, but dilated loops of small bowel suggested a partial mechanical obstruction of the lower small intestine. An upper gastrointestinal series demonstrated a normal stomach and duodenum with normal emptying time. However, there was such impairment of the passage of the barium through markedly distended loops of small intestine that twenty-four hours later, the contrast material still outlined these loops. (Fig. 4.) It was still present in both the ileum and colon at the time of surgery five days later.

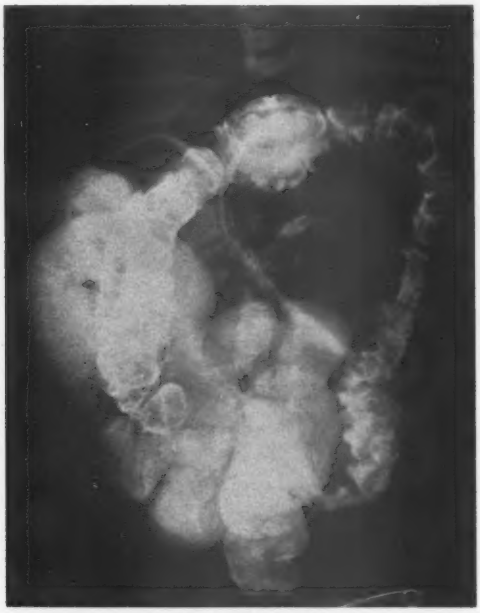

FIG. 4. Barium remaining in dilated loops of small intestine and in completely aganglionic colon twenty-four hours after being administered orally.

Physical examination of the baby at this time showed him definitely emaciated with a distended abdomen. Through the abdominal wall active peristalsis could be seen in dilated loops of bowel. There were no palpable masses or specific organs. Rectal examination was within normal limits.

With the preoperative diagnosis of partial obstruction of the small bowel at the ileocecal valve, a laparotomy was performed. The ileum was dilated, thickened and edematous down to the ileocecal valve, but the cecum was collapsed and appeared normal. A moderate amount of barium and fecal matter was in the rest of the large bowel. A side-to-side ileocecostomy was performed to bypass an apparent obstruction. The baby did well for the first six days, having passed two stools on the fourth day and one on the fifth. However, on the night of the sixth day he went into shock, became cyanotic, his abdomen more distended, and he died the following afternoon.

Postmortum examination showed a generalized peritonitis due to perforation of the anastomotic site. It was not until a secondary review of microscopic sections of the colon showed that there was only a rare ganglion cell that the true diagnosis of Hirschsprung's disease was made, the entire colon being involved.

CASE II. R. N. was a full term male infant who weighed 6 pounds, 11 ounces at birth. He initially

FIG. 5. Barium in colon thirteen days after barium enema.

took ½ to 1 ounce of formula but when only thirty hours old he began to vomit greenish brown mucus and fluid. He did this repeatedly for the next thirty hours, then at two and a half days of age he passed his first small meconium stool. He passed a larger stool on the third day and several on the fourth. An examination by barium enema at this time was reported to be within normal limits with a normal rectosigmoid and "nothing to suggest an aganglionic segment." (Fig. 2.) He then began to take his formula well, 1½ ounces every three hours, and was allowed to go home. He began to vomit again, therefore he was readmitted. His abdomen became distended and he obviously was not doing well. His formula was changed several times but there was no change in his condition. His symptoms were comparable to those of partial obstruction with active peristalsis. However, because he would retain several feedings at a time and continued to have three to five bowel movements a day, he was observed for several days. A roentgenogram of the abdomen at sixteen days of age showed unusual amounts of gas in the large and small bowel and some barium still in the distal colon. (Fig. 5.) Because the baby's condition was steadily deteriorating, an exploratory laparotomy was performed on the sixteenth day of life. A thickened, dilated, almost edematous appearing transverse colon was encountered with the descending colon the size of, and resembling small bowel. A right transverse colostomy was performed. When it was opened, the baby's condition improved dramatically.

The baby then did well except for some excoriation around the colostomy. His development was quite normal for the next eight months when the distal colon and, to a lesser extent, the proximal colon began to prolapse through the colostomy. In order to utilize this bowel before it became fibrotic, a Swenson pull-through procedure was performed when he was one year old. The aganglionic segment was found to include the sigmoid and descending colon up to the splenic flexure. The colon was transected several centimeters above this, but even though the colostomy was freed so that there appeared to be plenty of bowel to reach the anus, the colonic blood vessels would not reach that far. Therefore, the ascending colon was completely mobilized and turned down so that the transverse colon just to the right of the colostomy was anastomosed to the rectum 2 cm. from the anus. Thus, two-thirds of the transverse, all of the descending, all of the sigmoid colon, and most of the rectum were excised. The baby appeared to be in satisfactory condition at the end of the operation but he died six hours postoperatively.

Case III. J. DeR. was born on May 16, 1957, an 8 pound, 4 ounce boy after a normal gestation and delivery. He was transferred to Children's Hospital at the age of three days because of a history of vomiting all feedings for the past twenty-four hours. The vomitus was yellow or green in color. He repeatedly passed moderate amounts of meconium.

The family history was non-contributory. The mother had had three miscarriages and one stillbirth.

Physcial examination showed a well developed three-day old baby in apparent good health with no jaundice or dehydration. The abdomen was moderately distended without palpable masses. The baby would retain feedings intermittently and then vomit. He continued having moderate amounts of brown liquid stool three or four times a day. An examination by barium enema on May 20, 1957, showed much gas in the intestinal tract and no obstruction of the large bowel. However, there was almost complete failure of evacuation of the opaque enema after twenty-four hours. A distinct difference in caliber of the colon was noted at the splenic flexure, the transverse colon being approximately twice the diameter of the remainder of the colon distal to that point. (Fig. 6.) A diagnosis of Hirschsprung's disease with an extensive aganglionic segment was made. A laparotomy was performed when the baby was six days old. A large transverse colon was found with the descending colon difficult to differentiate from the ileum. A transverse colostomy was made and opened the following day. The baby began to pass frequent loose stools through the colostomy and promptly

Fig. 6. Funnel-shaped deformity at the site of transition of normal to aganglionic bowel at splenic flexure.

showed signs of being hungry. The next day he was started on oral feedings which he took eagerly and retained. He was discharged at two weeks of age, doing well.

His development was normal except for some irritation of the skin at the site of the colostomy. At ten months of age he began to have prolapse of the distal colon through the colostomy. A modified Swenson pull-through procedure was performed when the baby was thirteen months of age and weighed 25 pounds. In this patient, a more limited resection was carried out as a first stage, removing only the rectum and half the sigmoid, then turning down the ascending colon to perform the anastomosis between the right transverse colon and lower end of the rectum. The rest of the colon, consisting of the remainder of the transverse, the descending and part of the sigmoid, was left to be removed at a second stage. Postoperatively, this baby had a smooth course, except for recurrent boils on his left thigh. He is gaining weight and developing normally. He has four to five stools a day.

Case IV. R. D., a one and one-half month premature boy, who weighed 4 pounds and 12 ounces, began to vomit soon after he was started on oral feedings. His abdomen rapidly became distended. He was referred to the clinic service at the Children's Hospital of the East Bay when he was three days old. Physical findings included moderate dehydration with a weight of 3 pounds, 15 ounces,

marked abdominal distention and visible peristalsis in loops of the bowel seen through the abdominal wall. No obstruction was noted on rectal examination. Roentgenologic studies showed the presence of large amounts of air in both the small and large intestine, and an examination by barium enema demonstrated a funnel-shaped narrowing at the splenic flexure with the bowel collapsed from that point distally. The patient was treated with intravenously administered fluids and gastric suction. The following day, repeat x-ray films showed the contrast media was still present in the colon. A laparotomy was performed, a biopsy specimen of the sigmoid colon taken, and a transverse colostomy performed. On his sixth day of life, the colostomy was opened and the baby started on oral feedings which he took without emesis.

COMMENTS

Hirschsprung's disease should be suspected when signs and symptoms of incomplete obstruction develop in an infant or child. Procedures to establish a definitive diagnosis should be instituted early. These begin with a complete physical examination which shows the results of vomiting and distended intestines. Rectal examination is reported as being characteristic with an empty, snug rectum as though there was a stenosis just above the examining finger. However, the same sensation has been encountered with the actual obstruction being as high as the duodenum.

As the next step, a roentgenogram of the abdomen is taken. It will show excessive gas in the small and possibly in the large bowel but not in the lower part of the colon. An examination by barium enema will show a patent colon, and very likely the area of transition. Characteristically, a roentgenogram taken twenty-four or more hours later will show retention of barium in the colon, something the normal colon in an infant will not do. In one of our cases the funnel shape was demonstrated at only four days of life. A rectal biopsy may be useful in confirming the diagnosis.

Treatment consists of a prompt colostomy, preferably placed a short distance proximal to the transition of normal to aganglionic bowel. If not previously obtained, one may at this time obtain a biopsy specimen of the aganglionic area to confirm the diagnosis. When relief is not provided by colostomy in patients with extensive aganglionic segments, it is highly disastrous [6]. Swenson [7] even recommends early colostomies in babies with short segments in order to avoid the severe gastroenteritis to which these patients are subject. If the colostomy is not placed proximal enough to be in the normal colon decompression will not occur [8].

The definitive procedure, a Swenson pull-through, is delayed until the baby reaches the weight of 25 to 30 pounds. Accomplishing this operation during the first months of life has been tried elsewhere and abandoned because of the high mortality rate. Prolapse of the colon, such as occurred in our cases during the waiting period, should not cause concern as it caused no complications.

We were unable to anastomose the left transverse colon to the anus. This was not due to the length of the bowel, but rather to the inadequate length of the blood vessels in its mesentery. This is reasonable when one considers that with the transverse colon anchored high in the abdomen by the colostomy, the stimulus for growth of a long middle colic artery is not present as it is in those patients in whom the transverse colon may swing low across the abdomen.

Finally, as to the pull-through operation itself, we recommend a two-stage procedure. What is equivalent to an entire colectomy plus an anastomosis is required, and that is traumatic to a patient of any age. This can be divided into two separate operative procedures. At the first stage, only the rectum and a limited amount of the sigmoid are resected. The anastomosis is performed between the lower centimeter or two of the rectum and the ileum if the entire colon is aganglionic, or to the ascending colon if the aganglionic segment extends to the splenic flexure or higher. The two ends of the remaining colon are brought out as mucous fistulas until some time later when this segment is excised. Also, during a procedure of this magnitude, the usual techniques of gentleness, good anesthesia and meticulous blood replacement, which are so necessary to successful pediatric surgery, assume increased importance.

CONCLUSION

Four cases of Hirschsprung's disease with extensive aganglionic segments are presented and discussed. The clinical picture is that of partial obstruction of the bowel. X-ray films characteristically show: (1) excess gas in the bowel; (2) a patent bowel; (3) a change in caliber of the bowel; and (4) retention of barium in the colon for an unusually long time. Early

relief of the obstruction is mandatory. It is suggested that the definitive pull-through operation be performed as a two-stage procedure with meticulous attention to technique and blood replacement.

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DISCUSSION

Robert A. Scarborough (San Francisco, Calif.): Dr. Adams' presentation has been both interesting and instructive. His reported experience in four cases is sufficient to alert us all to the problems encountered in the exceptional case of Hirschsprung's disease with congenital absence of ganglia as far back from the anus as the splenic flexure or even the ileocecal valve. It is generally agreed that diversionary colostomy must be performed proximal to all bowel with absent ganglia. A proximal sigmoid colostomy will satisfy this condition in more than 90 per cent of cases.

We do need to recognize those cases in which colostomy must be performed in the proximal transverse colon, or in which ileostomy will be required because of complete aganglionosis of the entire colon.

Dr. Adams has presented fairly good evidence that perhaps we should be able to recognize the level of transition. In his first patient, with complete aganglionosis of the entire colon, laparotomy disclosed ileum which was dilated, thickened, and edematous. But the cecum was collapsed and appeared normal. The abrupt transition at the level of the ileocecal valve in this instance was so apparent that a diagnosis of organic obstruction was made. It is obvious now that this patient should have had an ileostomy.

In his other patients, Dr. Adams has described two signs to suggest the level of transition in ganglionic distribution: (1) Demonstration by barium enema examination of a funnel-shaped transition from dilated to narrow bowel of normal or smaller than normal caliber; and (2) recognition at laparotomy of a level of transition from dilated, hypertrophied bowel to that which appears quite normal on gross examination.

I must admit some lack of confidence in my own ability to determine accurately the level of transition without microscopic biopsy examination for determination of the presence or absence of ganglia. Such examination at multiple levels is still an important step in the final determination of the proper level for definitive resection of all aganglionic bowel. I have been particularly interested in Dr. Adams' original and successful use of a two-stage procedure in which, after resection of the rectum and rectosigmoid, he has performed a Swenson-type pull-through of the proximal transverse colon with primary anastomosis to a rectal cuff, and a later operation for removal of the remaining defunctioned abdominal colon.

Frederick H. Bentley (Portland, Ore.): This is a fascinating subject. I would stress the importance of recognizing the possibility of Hirschsprung's disease in a newborn with obstruction. Of the eleven babies I have operated on for this condition, two presented during the first week of life as having acute obstructions. The investigations did not suggest a mechanical block, and in each case transverse colostomy was performed with immediate relief. Later the disease was successfully treated by a resection and pull-through anastomosis.

As long as you have the thought in mind, that is all right, but the search for confirmation of the diagnosis raises the question of muscle biopsy. First, the pathologist may not have had much experience in staining and examining a frozen section for ganglion cells. It is all right if he has performed large numbers of these examinations, but the ordinary pathologist will tell you that he is giving you an opinion (as to the presence of ganglion cells) with some reservations.

Secondly, although we talk about aganglionic segments, it seems possible to have some cases of Hirschsprung's disease in which the colon is not completely aganglionic, but presents a reduction in the number of ganglion cells. In examining the sections you can find these cells here and there, but the segment of colon is not functioning properly

and the condition is later cured by a pull-through procedure, so that one assumes it was Hirschsprung's disease all the time. It is difficult for the pathologist examining a frozen section to make this assessment of the number of cells, and to give you a true opinion as to whether or not you are dealing with a reduction in cells. For this reason I find muscle biopsy as a diagnostic point confusing, and wonder whether Dr. Adams would be ready to comment on that problem.

Another point that is perhaps worth making is the development of the conus, an important x-ray diagnostic feature. With such a roentgenogram you know exactly what you have, but such a conus will only develop after a period of physiologic obstruction. The child is not born with it. If you perform a decompressing colostomy for Hirschsprung's disease early in the child's life, a conus will never develop, a lesson I learned some years ago.

We saw a baby at the age of two weeks in whom we strongly suspected Hirschsprung's disease. A series of roentgenogram showed the development of a conus. At first there was only a suggestion of a conus. One month later the conus was more evident. One year later there was a classic x-ray appearance; but it took time to get it.

The third point I would like to make briefly is to follow John Duncan's example and describe a case. This baby was born in Southern Oregon in 1930, and on the third day was taken into the local hospital with acute intestinal obstruction. He was operated on by the local general practitioner–surgeon who returned the child to his mother with the story that there was an acute distention of all of the bowel, and that no cause could be found and the baby would die.

I saw the mother in 1957, some twenty-seven years later. She tells the story that having received this judgment from the surgeon, although she was not a religious woman she decided to pray. She prayed that if strength were given her and the child could be saved she would devote her life to good works. Among the effects of prayer was the stimulus to the mother to give the baby repeated enemas, and she worked on her child until the fifth day after he left the hospital when there was a large fecal result. She continued working on that child and later on he worked on himself. He never had a bowel action in the next twenty-seven years without a whole series of enemas. He would be completely constipated for one month and would then finally fill a pail with his excrement.

He came to me at age twenty-eight. He obviously had Hirschsprung's disease, with flared-out ribs from the distention of the colon pressing the ribs out during the period of growth. We decided to operate on him to try to empty the bowel. We had little success. Photographs taken during the operation on the colon showed a narrow conus leading into a perfectly enormous colonic sac distended with solid feces. We managed to milk all the feces from the rest of his colon into the descending part, and to include that part in the area of resection. The resected specimen was weighed before and after emptying, and the difference in weight was ten and a half pounds!

It was easy to get rid of that enormous sigmoid and descending colon and bring the proximal end down. It was terribly difficult doing the anastomosis at the anus because of the disproportion. I had written to Dr. Swenson beforehand asking him whether or not he had ever performed this operation in adults. He replied saying, "Yes, it could be done with equal success in adults, but the operation was more difficult." I consider that the understatement of the century. This operation which ordinarily takes two hours in a baby, took six hours in the young man; and half that time was spent at the anal anastomosis. But the pull-through was completed, and normal healing followed. The man is now well with the most contented bowel in Oregon.

Remembering that he owes his life to the response and efforts of the mother shortly after birth, I am reminded of the words from the old hymn, that God moves in a mysterious way, His wonders to perform.

William F. Pollock (Santa Monica, Calif.): The first case described by Dr. Adams raises a question about the diagnosis. About ten years ago Dr. Wolf Zuelzer (*Am. J. Dis. Child.*, 75: 40–64, 1948) described a condition found at autopsy in babies in which the entire small and large bowel was aganglionic. The unusual appearance on the roentgenograms, the findings at surgery and the eventual fate of this child all suggest the possibility that this first baby had the condition Dr. Zuelzer described, and not a disease limited to the colon.

Possibly a review of the autopsy findings would make it possible to obtain some impression of the ganglion cells in the small intestine. The condition described by Dr. Zuelzer is invariably fatal and no form of surgical treatment has ever been successful in this disorder.

Harry E. Peters, Jr. (Oakland, Calif.): Because of my interest in the subject I would like to augment the discussion. Long aganglionic segments occur in only 10 per cent of the cases of Hirschspring's disease reported. It is interesting to note that some five to eight years ago there were practically no reports of patients with these long aganglionic segments. Now, in the larger children's hospitals, we find that obstruction appearing in the neonatal period due to long segment aganglionic Hirschsprung's disease is approximately as common as that of meconium ileus.

I think it is important to bear in mind when seeing these children in the noenatal period with an

obstruction, or with what clinically appears to be an obstruction, that although they are passing meconium they are at the same time vomiting bile.

I would also like to emphasize again that in the newborn, during the examination by barium enema, we do not have a sharp division between the aganglionic and the dilated segment above, but rather a cone-like area which is easy to miss. Sometimes we have to rely on the film taken twenty-four hours later which reveals that the barium has not been passed.

Incidentally, one can almost categorically state that if an infant in the neonatal period appears to have an obstruction, and at the time of the barium enema one can see that the barium passes from a narrow to a more dilated segment (one must rule out the presence of a meconium plug), this is diagnostic of Hirschsprung's disease, and biopsy is probably not necessary.

I would like to mention, the importance of performing a colostomy in the neonatal period on any child in whom a diagnosis of Hirschsprung's disease has been made. This is essential because of the danger of subsequent development of bacterial colitis. These children are all susceptible to bacterial colitis, and you may lose the child if a colostomy is not carried out in the segment just above the area in which ganglia are absent. Finally, some children in whom a pull-through operation has been performed, although uniformly the results are good, will still continue to have recurrent attacks of bacterial colitis. Attention may also have to be paid to seeing that additional care is rendered relative to enemas and catharsis in spite of a successful operation.

Siegfried F. Herrmann (Tacoma, Wash.): I think we should all be grateful for the presentation of this subject, because failure to recognize and treat such cases is a terrible tragedy.

I would like to mention a boy who was born fifteen years too soon, before Swenson and before pull-through operations.

I saw this little fellow in 1937 when he was two years old. He had typical Hirschsprung's disease.

Two years earlier I had been asked to see a little girl, his sister, in whom this evidence of neonatal obstruction had developed. We thought she had an acute mechanical obstruction. I operated on her and found only thickened descending colon and a normal looking lower sigmoid colon. I did not know just what it was and I said to the pediatrician. "I think the only thing I can do with this is try to anastomose the dilated bowel to the part that looks normal."

We tried to do that, but peritonitis developed and the baby died. Evidently this was Hirschsprung's disease.

The boy was the second baby in this family—this points up the fact that this condition can be familial—and had what we recognized as Hirschsprung's disease. By this time I thought I was a little wiser because I had been reading about Dr. Adson's emphasis on sympathectomy in the treatment of Hirschsprung's disease.

Previously treatment had not been very satisfactory. Dr. Adson advocated sympathectomy with the idea that somehow the inhibiting influence on the distal bowel would be removed by sympathectomy and the colon then would function. That was the proper procedure in those days.

I performed a sympathectomy on this boy, and I thought he benefited by it. When I first saw him at the age of two he had an abdominal circumference of 24 inches. Five months after the operation his abdominal circumference was 21 inches, a reduction of 3 inches. He was having bowel movements although the mother frequently gave him enemas; sometimes the bowels moved spontaneously.

I saw the boy again about a year later. At that time his abdominal circumference was still 21 inches. The mother was quite satisfied and believed his condition was improving. At times his bowels did move spontaneously.

I lost track of him until he was about ten years old when I saw him walking with his mother. She stopped me and said, "Doctor, this is Harry. Do you remember him?"

I did remember him and he looked fine. He apparently was getting along well.

I heard nothing more about Harry until recently when I learned he had died at twenty-two years of age. He had been married for a few years, and his wife came to my office to see my partner for an examination incidental to her employment. She told my secretary that her husband had been a patient of mine.

I immediately became interested to find out why he had died. If you could have seen the pictures of this man that the pathologist took at the time of autopsy, you would see how important it is to treat Hirschsprung's disease properly.

From what I could learn, the patient had gone to a movie and had eaten a bag of popcorn. His abdomen became so tremendously distended and he so uncomfortable that he was taken to the hospital. In spite of attempts to ease his condition with enemas and rectal tubes he died.

I asked the pathologist for the cause of death. He said, "He died of Hirschsprung's disease due to distention. His lungs were completely compressed and his heart was so embarrassed by this distention that it killed him."

The pathologist took pictures to show the tremendously dilated abdomen and colon. I have never seen anything like them. The loops of colon were 6 or 8 inches in diameter. The entire abdomen was filled with colon and air and feces.

This man died because he did not have the proper operation. His wife said he had visited some twenty docotors; none of them had ever helped him and apparently none of them knew how to help him.

In 1950 I heard Dr. Swenson talk about this subject in Boston. He mentioned over sixty cases of Hirschsprung's disease in which he had performed the pull-through procedure. Dr. Swenson has made it possible for us to cure this condition in babies, as I have done in other cases. I just had to describe what can happen in a case of Hirschsprung's disease if the condition is not corrected.

BURTON ADAMS (closing): I am glad there was this much interest in a subject which I have found so interesting.

Regarding Dr. Scarborough's comments about the problem of the short vessels, there appears to be a logical explanation. The transverse colon in these babies has been anchored in the upper part of the abdomen by the colostomy since just after birth and the stimulus for a long middle colic vessel to grow the way it does in babies who have a free, low-hanging transverse colon is absent. In our baby the vessels just would not reach far enough to bring the transverse colon down to the anus.

Relative to Dr. Bentley's discussion regarding the diagnosis of such cases by biopsy, our present pathologist (Dr. James McAdams) uses two factors, the complete absence of ganglion cells between the circular and longitudinal muscle layers and the presence here of relatively large nerves.

Dr. Pollock commented on a completely aganglionic bowel. Last Fall in Chicago Dr. Swenson stated that he was aware of a case reported in England of a completely aganglionic bowel, and also that cases in which areas of aganglionosis have been present in the small bowel have been discussed with him by several people.

I want to thank Dr. Peters for his permission to use the first and fourth cases. He was the consultant on these clinic cases.

The Use of the Electronic Segmental Plethysmograph and the Digital Plethysmograph in Arterial Surgery

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IN the past ten years many advances have been made in the technic of arterial surgery. Diseases previously considered beyond the scope of satisfactory medical treatment now have a number of highly satisfactory solutions and new operative technics are widely used. In the evaluation of patients with arterial problems, however, there has been a rather noteworthy lack of satisfactory methods for accurate studies. It would seem especially valuable to avail ourselves of a method of objective and easily compared studies for the postoperative evaluation of results since one prominent vascular surgeon recently reported a 96 per cent successful result from his by-pass grafts, while a panel of experts just agreed that 50 per cent success is the common experience.

Physicians are at the present time relying upon limited information obtained by physical examination, the somewhat inaccurate evaluation of the patient's subjective reactions to lumbar sympathetic block and his actual performance after blocks, or the rather complicated process of arteriography. Arteriography, to be sure, has many irreplaceable indications in the study of arterial disease and will continue to a limited degree to be necessary in spite of its many drawbacks and dangers. The variety of complications from arteriography or aortography have been well documented in recent years [*1,2*]. It is our feeling that the information obtained by arteriograms in many instances is quite misleading as to the actual condition of vessels, as well as the functional dynamics of the arterial tree. This is due partly to the fact that the vessel being studied is usually placed in a state of spasm by the very performance of the arteriogram itself.

In the past three and a half years we have had the opportunity to evaluate arterial disease by the means of digital plethysmography and the use of an electronic segmental plethysmograph. The plethysmographic studies have been carried out with the Winsor model digital plethysmograph [*3*] employing a four-channel writing apparatus.* (Fig. 1.) Basically this instrument measures the volume of flow into the tip of a digit including exactly 4 cc. of tissue through application of plastic cups. The pressure and the volume changes are recorded through a differential pressure chamber serving as an electrical transducer, an amplifying circuit and a recording writing mechanism. The plethysmograph also is provided with means of recording accurately, in a manner that can be repeated for future comparison, the magnitude as well as the shape of pulse waves at any level on any extremity. (Figs. 2 and 3.) The apparatus also provides for the recording of temperature changes by means of thermistor needles attached to the digit and recorded on a calibrated temperature scale on the graphic paper. Simultaneous pulse wave readings may be obtained at separate levels on both lower extremities and one upper extremity with blood pressure-type cuffs applied first at the level of the groin, then above the knee, below the knee and at the ankle. Accurate information can be recorded as to the relative magnitude of a pulse wave as well as the exact form of this wave. In this manner one can determine quite accurately the level of obstructions, total

* Electro-Medical Engineering Company, Burbank, California.

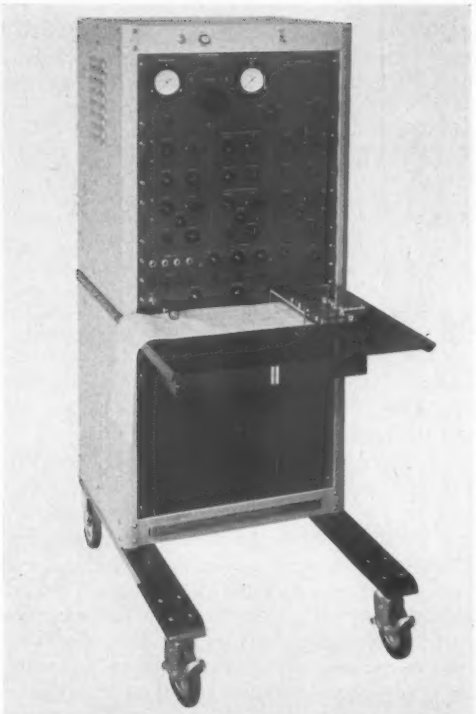

FIG. 1. Current model of the four-channel vasograft (Winsor) which combines the segmental plethysmograph and the digital plethysmograph with four simultaneous writing channels. Accurate measurements of blood pressures, digital blood flows and temperature changes can be accurately recorded.

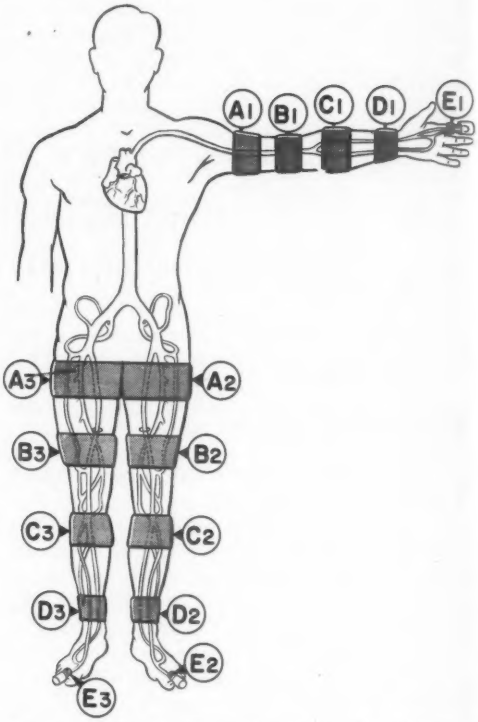

FIG. 2. Mannequin illustrating the usual positions of placing the plethysmograph cuffs and the digital cups. (From: WINSOR, T. [4])

or partial, in major arteries. One may, from this data, infer the exact nature of a patient's disease and know whether such clinical phenomena as intermittent claudication or pregangrenous changes of the toes is due to a single or multiple block in the arteries, or whether it is due to a general obliterative process which progresses down the arterial tree. After this preliminary scanning of the pulse waves of an extremity has been accomplished, accurate information about specific flow in the toes may be obtained by the use of the plastic cups on the toes. After digital pulses have been recorded and a base line established, a blood pressure cuff on the leg is raised instantaneously to well above the normal venous pressure (usually 60 mg. Hg), so that any inflowing blood into the digit will remain trapped and the volume of the digit will increase with each systole. This produces a rise of the base line and the actual digital flow in cubic millimeters per second can be determined from this graph. (Fig. 4.) These flow studies are done under basal conditions when the patient is in a quiet, sound-insulated room with minimal temperature changes, lying comfortably on a bed in a hospital gown, and with a soft musical background provided. The effect of vasodilatation upon the arterial circulation is then studied after thirty minutes of general body heating with an electric blanket and the ingestion of 2 ounces of whiskey. If the arterial tree initially has been in some degree of spasm or if the collateral circulation has not been completely opened, these facts are demonstrated by the increased digital flow after general vasodilatation. If one is seeking to learn the actual effects of sympathectomy upon the diseased extremity, the circulation to the second toe is placed in the maximum state of dilatation by means of a simple posterior tibial nerve block with a local anesthetic agent. Since

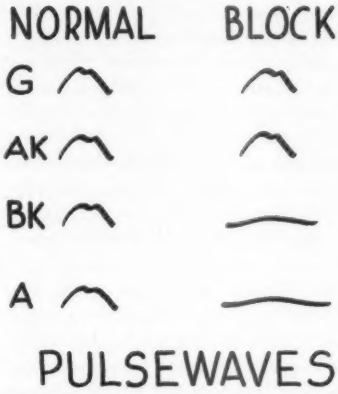

FIG. 3. Diagrammatic representation of single pulse waves obtained by the segmental plethysmograph both with normal circulation and in a patient with a popliteal artery block. G = groin; AK = above knee; BK = below knee; A = ankle.

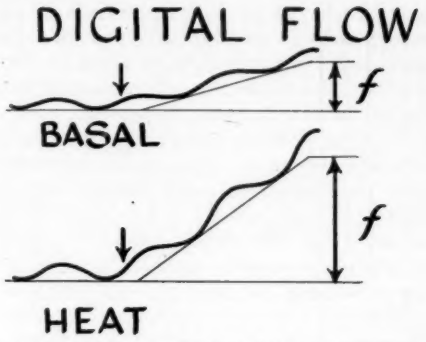

FIG. 4. Graphic representation of the measurements of digital blood flow. Along the pulse tracing at the arrow, venous outflow from the foot is instantaneously occluded by a cuff. The rise of the base line, noted as a small letter *f*, represents the increase of volume and can be measured accurately to 0.1 cu. mm. per second of digital flow. Notable increase in this flow from the vasodilatation secured by the application of body heat is shown in the lower curve.

the establishment of the vascular test center at Mercy Hospital, a total of about 1,100 patients have been tested in the manner just described. From this experience we believe we can evaluate quite accurately the nature of the patient's arterial obstruction. Correlation between the vascular studies obtained in this center and the findings at surgical operations has given us increasing confidence that much of the previously existing guesswork has been eliminated in diagnosing these patients and in following their post-treatment courses.

A second apparatus which has been most useful is a segmental plethysmograph, devised by Dr. Winsor, which is small, readily portable and therefore easily available in the patient's room or in the operating room. This consists of a

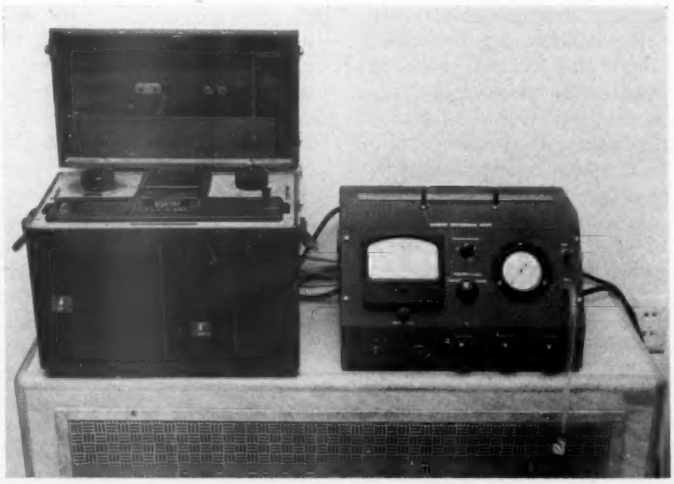

FIG. 5. The portable Winsor model of the segmental plethysmograph with its attached electrocardiographic apparatus is used for recording purposes. This small unit is used at patient's bedside and in the operating room to demonstrate the location of arterial blocks and the magnitude of flow at different levels of the extremities.

single blood pressure cuff connected to a pressure transducer system and provided with amplifications of from one to eight times the actual electrical output of the transducer. (Fig. 5.) In this manner it is possible to detect pulse waves which, although actually present, are too weak to be appreciated by unaided finger palpation. This apparatus has been available at the patient's bedside within a few minutes after the occurrence of suspected arterial emboli and the presence or absence of such a vascular accident proved beyond any question. We have also routinely applied this instrument in the operating room following major arterial surgery, the resection of aneurysms, the removal of previously located emboli or the opening of the diminished arterial lumen by thromboendarterectomy. Here, for the sole purpose of establishing the presence of pulse waves, the instrument is used as an electronic oscillometer. The segmental plethysmograph aids in studying the anterior scalenus syndrome. The plethysmograph can be used in measuring the amount of blood flow into muscles of the calf [4].

A number of specific problems of arterial disease will illustrate the application of the testing methods previously enumerated.

ARTERIAL EMBOLISM

In the past it has been a common experience among physicians that arterial emboli all too often are not diagnosed until irreversible changes have taken place both within the occluded artery and in the peripheral tissues. All of us have observed patients who have had a sudden initial complaint of severe pain, inability to walk, coldness of the extremities and an absence of peripheral pulses, often associated with auricular fibrillation, in whom the severity and the exact location of an embolic block could not be diagnosed quickly and accurately. It is common that the initial severe pain and color changes seem to improve in a few hours, thus giving both the patient and the physician a false sense of improvement.

Since the plethysmograph has been available to study patients in the hospitals, and on two occasions in a patient's home, we have decreased the previous long delay of diagnosis to an average time of about only three hours from the occurrence of initial symptoms to the actual removal of the embolus. One of the earlier patients so examined was a sixty-five year old woman who was undergoing an uncomplicated convalescence following renal surgery. This patient had a long history of mitral stenosis which had not handicapped her. She had experienced fibrillation for about eight years. On the fifth postoperative day the patient noted sudden severe pain in both legs, more marked on the right. Her internist was in the hospital at the time this occurred and saw the patient immediately. On telephone conversation regarding the patient's condition, it was suggested that a study with the segmental plethysmograph be carried out. An unequivocal diagnosis of bilateral block implying a saddle embolus was available in graphic form by the time she was examined by the surgeon. The operating room was immediately alerted and in a matter of fifty minutes from the time of the occurrence of the pain laparotomy was performed and a large saddle embolus removed. Following the closure of the arteriotomy incision, cuffs placed below the knees bilaterally were used to study the distal circulation. On the right side it was noted that no pulsation could be recorded below the knee. The cuff was advanced cephalad and at a point a short distance above the knee adequate arterial pulsations were noted. With this positive evidence of popliteal artery block the laparotomy incision was closed, the patient placed in prone position, the popliteal artery opened and a second embolus removed from this site. Had complete dependence been placed on the digital palpation of the pulses or the observation of the skin temperature changes, the second popliteal embolus would certainly have been overlooked, for unaided physical findings were not notably different even after the second embolus had been removed even though the plethysmographic tracing clearly demonstrated the return of pulsations at the level of the ankle. It has been commonly observed by surgeons that palpable pulsations often do not reappear, particularly in distal vessels, for forty-eight hours or more following surgery. This probably is due to the presence of severe vasospasm incident to the trauma of the arterial surgery at a higher level. If such unrecognized embolism or thrombosis goes untreated, the opportunity for re-establishment of satisfactory flow may be lost entirely. With the segmental oscillometer, tests are usually carried out at the patient's bedside daily for at least seventy-two hours after surgery. If severe endarteritis is

known and one is therefore concerned about the possibility of late slow thrombosis, these tests naturally are carried out for a longer time. In the course of the last thirty-one arterial embolectomies performed on our surgical service, three patients had symptoms of over fifty hours' duration (seventy-four hours in one) from time of onset of pain until surgical relief of obstruction. There is naturally considerable distal thrombosis in these instances and the plethysmographic information as to the presence or absence of complete restoration of distal circulation here is even more valuable. On two occasions with the long-standing periods of embolization it has been necessary to perform retrograde flushings through the posterior tibial artery, as suggested by Crawford [5]. By this technic a number of small thrombotic particles have been removed and satisfactory restoration of circulation achieved. In some instances the demonstrable pulse in distal vessels has amounted to a very low amplitude wave, even with an amplification of eight times the electronic output of the apparatus. However, we are usually able to accept this as evidence of a definitely patent lumen with extreme spasm and have accurately anticipated gradual improvement within the first forty-eight hours after the operation. Since instituting the operating room-testing of all patients following arterial surgery, there has been no instance of gangrene or loss of any part of the limb even with the cases of long duration mentioned previously [6].

AORTIC ANEURYSMS

We have felt it important to study patients with aortic aneurysms preoperatively to determine the actual status of distal circulation, as well as to have some information as to the possible necessity of concomitant endarterectomy. If we can anticipate a satisfactory run-off in the distal tree, we should not anticipate major circulatory problems following the placing of a graft. As in the operating room-testing of patients treated for embolism, we have also placed cuffs below the knee bilaterally on all patients with abdominal aneurysms. In three of the past thirty cases of abdominal aneurysms, secondary embolic blocks have been found at the level of the popliteal arteries which were not present immediately before the abdominal incision was made. This has meant that we have inadvertently broken off either arteriosclerotic plaques or a portion of the organized thrombus during the operating procedure. Most of these patients have such poorly palpable dorsalis pedis and posterior tibial arteries that these pulses were not palpable prior to surgery, and recognition of these operative emboli would have been impossible without the help of the oscillometer.

ARTERIOSCLEROSIS WITH OBSTRUCTION

Perhaps the most valuable use we have found for the complete vascular studies has been in the evaluation of patients with obliterative endarteritis. It is possible from these studies to determine whether or not this is segmental in nature and therefore amenable to local endarterectomy or by-pass graft or whether the disease is of a diffuse progressive nature from the groin downward [7]. In many instances of this type of disease, however, it has been possible to demonstrate that although collateral circulation was present it was not fully functional until adequate dilatation had been obtained. One sixty-seven year old man complained of severe intermittent claudication, had pregangrenous changes of the toe and had upon one occasion been tested and showed no evidence of improvement of digital flow under vasodilatation by general body heating and ingestion of whiskey. He was first seen by us three months after this first test had been made, and it was suggested that re-testing be carried out, this time adding posterior nerve block to the procedure. It was most gratifying to find that despite the evidence of severe arteriosclerosis not amenable to arterial surgery, the digital flow improved almost to a normal level following this block. Accordingly, lumbar sympathectomy was performed. The patient's ulcerated toe has healed and his claudication has disappeared; he has made a quite satisfactory recovery. If one finds consistently damped waves from the level of the groin downward, it can be predicted that the person will have a block either high in the femoral artery or in the iliac. (Fig. 6.) In such instances, because it is not possible to test at a higher level, an aortogram is usually of value in determining the exact position and length of the block. We occasionally use arteriograms in the femoral vessels to determine whether or not the length of the block would make endarterectomy or by-pass graft the more satisfactory treatment. In studying the Leriche syndrome one cannot only

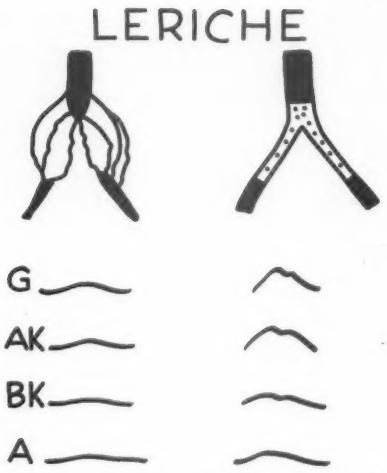

FIG. 6. Diagrammatic representation of the uniformly damped waves in the lower extremities in a patient with the Leriche syndrome, as shown on the left, and the restoration to normal wave forms after the placement of a bifurcation graft, as shown on the right.

demonstrate the fact that there is a bilateral impaired flow in the thighs, but also can study the nature of the circulation in the serial stations to the level of the ankle and predict the probable degree of total peripheral restoration of flow. About forty cases of obliterative diseases have been found suitable for surgical correction by such studies.

VASOSPASTIC DISEASES

The evaluation of circulation impaired because of pure spasm of vessels or of diseases in which spasm plays an additional important role can be studied with great accuracy with the tests described. The study of Raynaud's disease reveals diminished pulsation and decreased flow in the digits and the satisfactory return to normal levels following the general vasodilatation or localized vasodilatation on the basis of sympathetic blocks. It has been possible to determine the element of vasospasm following trauma to the extremities and specifically to predict that some of the patients who have pain after crushing injuries have critical circulatory insufficiency. We can demonstrate specifically that great spasm does exist, and accordingly early lumbar or upper thoracic sympathectomy can be performed very early in the course of the disease without waiting for atrophic changes to appear to prove the existence of reflex dystrophies. A four year old child sustained a very severe crushing injury to the leg from the midthigh downward, two compound fractures and extensive damage to the skin. Only three toes showed no evidence of severe tissue destruction but the color was poor. It had been originally believed that above-knee amputation would be necessary but the demonstration of the digital flow and actual pulsatile waves in these toes was proved beyond any doubt by means of the plethysmograph cup on the toe. On the basis of this definite evidence, instead of performing low thigh amputation as the orthopedist had suggested, the extremity was débrided and grafted. The child did lose some portions of muscle but at the present time, three and a half years after injury, is walking fairly satisfactory and should be able to obtain complete growth length of the extremity. The plethysmograph has also been most useful in studying gunshot wounds, compound fractures and other similar injuries to determine not only the exact site of the interruption of arterial flow but also to prove again the competency of circulation after surgical treatment has been completed.

SUMMARY

A method of arterial testing has been described which has enabled surgeons to evaluate accurately the nature of patients' arterial disease, the exact segments of obstruction and to suggest the optimum method of correction, whether this involves embolectomy, grafting, endarterectomy or sympathectomy, and to evaluate instances of traumatic arterial injuries. We believe that this system is reliable, is not attended by any hazard in its performance, and in essence has removed from the evaluation of arterial problems most of the guesswork under which we labored in the past.

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DISCUSSION

Roy Cohn (San Francisco, Calif.): Plethysmography is a comparatively old form of physiological measurement, having been first reported in 1732. According to the literature, a proper plethysmograph has the following nine criteria: (1) The pressure in the pneumatic system should change 0.5 mm. of water or less for every 50 cu. mm. volume change. (2) It must be standardized accurately against a known volume. (3) It must reproduce faithfully the pulse wave contour of a normally pulsating digit. (4) It must be highly sensitive so that 10 cu. mm. volume change will deflect the stylus 50 mm. (5) The frequency response should show less than 3 per cent decrease in amplitude at 5 cycles/second. (6) It must give a linear amplitude response with an accuracy of plus or minus 2.5 per cent to a 50 mm. induced volume change when set at standard sensitivity. (7) It must have two proper speeds at 25 and 2.5 mm./second. (8) It must have a rapid warm-up period and be essentially free from drift. (9) It must be free of microphonic and alternating current interference at full sensitivity.

Dr. Winsor, who set down these criteria, believes that his apparatus meets all these requirements. However, when one reads the arguments among the physiologists over such a relatively simple phenomenon—such as after a drop in the venous occlusion plethysmogram and the question of whether there is a reflex vasoconstriction elicited by distention of the local veins (as suggested by Gaskel and Burton in 1953)—it is difficult to believe that the data obtained by this method are as forthright as Drs. Steelquist and O'Connell suggested.

My own experience with this method has been so slight, however, that I am willing to yield to the authors' far greater experience.

Frederick H. Bentley (Portland, Ore.): I would like to express a word of caution in this field and will confine my remarks entirely to the second part of the paper, that on oscillometry, the measurement of the pulse wave as an expression of arterial flow. Some of the best minds in medicine have been working in this field, as Dr. Cohn said, for a long time, and the longer they work the more cautious they become in interpreting the physical results of the machine.

When you take the transmission of a pulse wave from the center of a limb to a pneumatic cuff encircling the limb at that point, there are many physical variables to consider, of which I will mention just two. The first is the girth of the limb. The thicker the limb and the more fat there is, the more only the peak of the pulse wave will come through and not the base of the pulse wave, so that you get an apparent narrowing on the oscillometer result, which is not related at all to flow but only to the medium through which the pulse wave is travelling.

A second variable is the width of the pneumatic cuff encircling the limb. Von Recklinghausen, in his classic paper in 1901, when he was working out the data on which we base our sphygmomanometer blood pressure readings, showed that with narrow cuffs there was not good correlation between the pressure at the center of the limb and the pressure recorded in the cuff. This was done in 1901 and was repeated and expanded following the war, by Thomson and Doupe in Winnipeg, who confirmed that the cuff needed to be at least 4 inches wide if there was to be good correlation between the pressures at the center of the limb and in the encircling cuff.

Such variables make it permissible to accept a positive result from the oscillometer, and less satisfactory to accept a negative result. In fact, a negative result may only be interpreting the characteristics of the method. That is one aspect of the problem.

The second is the problem of continuous flow. It is possible to have a degree of arterial obstruction sufficient to obliterate the pulse wave without stopping the flow through the artery. I had that forcefully brought to my notice in 1940 when I was working for the Medical Research Council and we were studying pressure injuries to the limbs. We would put a narrow cuff around the root of the limb and blow it up to 300 mm. Hg and then, on opening the popliteal artery to cannulate it, to our great surprise find a large continuous flow of blood coming through this pulseless artery. This caused me to read the literature!

In such a case there is sufficient arterial obstruction to obliterate the pulse wave but not enough to obliterate the flow. In spite of a large continuous flow, the oscillometer would show an apparently negative result. Sharpey-Schafer and his colleagues in London have worked on this problem and have shown by measurement that when blood flow is low the oscillometer does not give a true indication of the volume of flow. When the pulse wave on the oscillometer is poor or absent all you can safely conclude is that there is no pulse wave at that particular point, which is not quite the same thing as saying that you have not got a considerable flow of a continuous nature.

I hope I have not been too negative in regard to this stimulating presentation but this is a subject in which a positive result can mean something and a

negative result may mean that the machine has limitations.

J. Howard Payne (Los Angeles, Calif.): I wish to compliment the authors for bringing to the attention of this Society a very useful, versatile, sensitive and reliable instrument, the segmental plethysmograph. This instrument must be differentiated from an ordinary oscillometer which merely records pulsations of a limb or digit in arbitrary units.

The plethysmograph assists in locating obstruction in the arteries, determining the rigidity of the arterial walls and measuring pulse velocities. The fact that the instrument can be standardized makes it possible to eliminate error because of differences in the size of the occluding cuff, volume of the part, amount of air in the cuff, different applications of the cuff, degree of tightness of the cuff and the different technicians. The plethysmograph is highly sensitive and after standardization consistently gives recordings of pulsations in patients with peripheral vascular disease who do not have palpable pulses at the ankle or foot. It is possible to increase the sensitivity eight times. This is important in studying patients with far advanced arterial disease.

During the past five years we in Los Angeles have been interested in following the progression of chronic occlusive disease in patients who have been treated with medication and diet, direct arterial surgery with or without sympathectomy, and those who have had no treatment at all. I am certain our concepts of the natural progression of this disease and its predilection for certain segments of the arterial tree are going to be altered by a final analysis of these studies.

John H. Steelquist (closing): I do not wish to imply that we are getting any better results than Dr. Cohn; we, too, have our headaches. However, we do believe that this bedside re-evaluation has been of extraordinary value in caring for patients after arterial surgery.

Perhaps one of the things that has helped us is that we have learned to believe this tracing to the degree that if the machine indicates there is no blood flow and the surgeon's finger implies there must be, we will believe the machine. So far, in every instance in which we decided we must reoperate upon a femoral or popliteal artery to remove a clot after aortic surgery, we have found that the tracings were correct in reflecting the fact that something had happened subsequent to surgery. This may have happened on the operating table, for you cannot tell whether you have dislodged an endarterial plaque or a clot forming an embolism, or it may have happened a week postoperatively in the hospital.

Dr. Bentley, I think, has pointed out the basic factor that none of these machines is foolproof. Going back to Dr. Cohn's remarks, there are no real miracles obtained with this machine. It actually reflects phenomena parallel to what Dr. Bentley suggests we would like to do, that is, measure directly the flow within a vessel itself. However, it has been quite valuable to be able to say that now we know things are a little worse or better, or certain other phenomena are occurring. There is in the literature, of course, a great deal of information about this and other machines. Dr. Winsor has many published reports in which he has also studied the matter of the width of the cuffs and the nature of the flow.

Dr. Payne's remark about being able to standardize tracings and compare them is quite true. A number of patients have been tested both in his center and in ours, and it is very difficult to pick up any significant difference in the tracings made with two machines and two technicians. For example, one of our patients went to Chicago for consultation on obliterative arterial disease, taking with her the reports from Dr. Winsor's laboratory and the reports from ours. After they were studied, we were requested to send ours, because the tracings appeared to be identical copies rather than studies from two separate laboratories.

Absent Aortic Arch and Other Variants of Coarctation

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EXCISION of the narrowed segment with anastomosis of the aorta has come to be the accepted technic for relief of coarctation. Early in the history of the operation there were recommendations for mobilization of the left subclavian artery, swinging it downward in some instances to effect an anastomosis [1–2]. The literature also has carried suggestions that grafts occasionally are required to achieve restoration of vascular continuity.

Such precautions came to seem less and less pertinent to us in the course of operating upon approximately sixty patients. Adequate exposure, careful mobilization of the vessels, and occasionally oblique section at the site of anastomosis in order to secure a sufficiently wide lumen seemed to be the sole requirements to be met. More experience and more ingenuity in shaping the vessels indicated a greater and greater applicability of the basic operation. Even in four instances in which there were coexistent coarctation and patent ductus arteriosus there was no insuperable surgical problem. The only matter of real concern was the elevation in pulmonary arterial pressure to which the patient had been subject.

Grafting is also not easy to accept without qualification. It may be considered an undesirable complication to the operation, both on the basis of mortality [3] and because, especially in children and in adolescents, one has a strong desire to use the patient's own tissues rather than take a chance on homologous human tissue or synthetics which may not endure for a long span of life.

In the next ten cases in a consecutive series there were three instances in which it became all too evident that dependence on a single surgical technic would not suffice. It was established also that the acceptance of the findings from a routine physical examination and roentgenogram of the chest might require considerable amplification if there was any suspicion of an extraordinary abnormality. The purpose of this paper is to report what seemed to be two important variations in the over-all picture which have not been encountered widely and which resulted in a fatal outcome in the management of these patients. The third is presented briefly to indicate how a more thorough preoperative investigation and a modification of anesthesia and surgical technic resulted in an entirely satisfactory recovery.

Both failures with subsequent mortality occurred in patients in whom the distal aortic segment anastomosed to the proximal aorta proved inadequate to the great pressure which was established by open communication. In retrospect, the simple fact is that such thin, fragile vessel walls should not have been expected to be equal to the pounding which the pulse pressure necessarily causes when there is direct communication with the aorta. The fundamental evaluation of the tissue strength was largely one dependent on the surgeon's judgement and did not require laboratory confirmation.

CASE REPORTS

M. L. was first seen at the age of five years at the Children's Orthopedic Hospital (Seattle) in 1953. She had been referred because of a complaint of headaches. Her doctor had noticed "pounding" carotid pulsations in the neck bilaterally, but he had been unable to palpate any pulses in the four extremities. Her early growth and development were not remarkable. The only additional finding before her appearance at the hospital was that of a broad mediastinal shadow on the x-ray film, particularly on the right and superiorly near the root of the neck. Physical examination at the time of

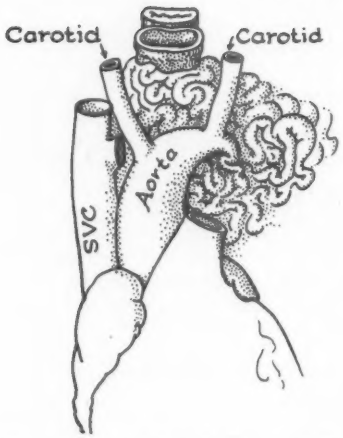

FIG. 1. Case 1. Anterior view showing ascending aorta, carotid arteries, and angiomatous mass.

admission confirmed the presence of bounding carotid pulses and also the lack of any palpable pulsations in the four extremities. There was no abdominal aortic pulsation. It was obviously impossible to determine arterial pressures in this instance by the use of a cuff. Efforts to do so by direct puncture were inconclusive technically, but certainly seemed to indicate a very marked degree of hypertension within the carotid vessels. An attempt at retrograde carotid arteriography had to be abandoned because of profuse hemorrhage and shock. The child's carotid artery, which was very friable, was closed with some difficulty after failure in an attempt to insert a catheter both for investigating the pressure within the vessel and for injection of a contrast medium.

Subsequent angiocardiography of the venous system was considered unwise because of the large number of allergies and sensitivities which the child was observed to have. She was followed up until June 1957 when increasingly severe headaches made it seem wise to perform right thoracotomy in an effort to establish the true state of affairs. At operation it was discovered that there was an ascending aorta with carotid vessels extending into the neck on both sides, but no aortic arch in the orthodox sense. (Fig. 1.) The mass which caused the shadow in the superior mediastinum on the right proved to be a large collection of blood vessels in a sort of hemangioma. Dorsally from the root of the neck there extended downward on the right side a vessel more than 1 cm. in diameter which at the level of the lower border of the third thoracic vertebra widened into a typical descending aorta with intercostal branches. This vessel, extending downward and presumably constituting the principal proximal source of blood to the descending

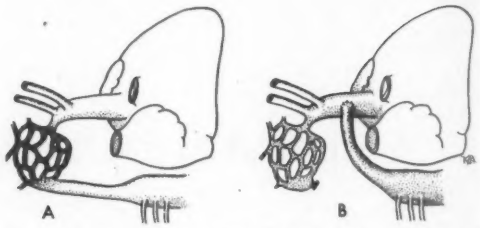

FIG. 2. Case 1. Lateral view showing section of slender vessel from neck with anastomosis to ascending aorta. A, preoperatively. B, postoperatively.

aorta, might have been considered as a prolongation and dilated form of a vertebral artery on the right side. (Fig. 2.) It was decided to employ this vessel to construct an arch by cutting it near the root of the neck and swinging its upper end forward to the ascending aorta. This was accomplished by passing the vessel lateral to the trachea and esophagus, but medial to the superior vena cava. At operation the vessel seemed rather fine and thin, but it was thought to be of sufficient diameter to establish what was considered an adequate flow for satisfactory delivery of blood to the torso and to the lower extremities. Nothing could be done to establish a normal vascular pattern to the two upper extremities. Immediately after the anastomosis was completed and the clamps removed there was the appearance of a pulse in the descending aorta. Postoperatively the child had femoral pulsations as well for the first time in her life. Her early recovery was satisfactory and on the tenth postoperative day she was discharged from the hospital and returned to her home in a neighboring city. Roentgenograms taken during her hospital convalescence did not indicate anything but a gradually resolving atelectasis in the right lung.

On the fourteenth postoperative day she was readmitted to the hospital with a complaint of nausea and vomiting of about eight hours' duration and with one episode of hematemesis. Within an hour she suddenly died. Autopsy revealed a patent suture line which was intact, but a ruptured aneurysm of the thin aortic segment which had been converted into an arch and which proved to be totally inadequate to withstand systemic pressures.

The second case was that of a twelve year old boy who was seen because of hypertension in the upper extremities and the absence of pulses in the abdominal aorta and elsewhere through the lower part of his body. The preoperative laboratory findings and roentgenograms of the chest were within normal limits. The blood pressure in his upper extremities was 160/100 mm. Hg. In short, he appeared to have an ordinary coarctation.

At operation in June 1956, he was found to have a coarctation consisting of the complete diaphragm.

(Fig. 3.) The obstruction lay at the upper end of a thin segment of aorta extending as a cylinder .5 cm. in diameter downward for a distance of 3 cm. to a tapered, considerably thicker, descending aortic segment where the attachment of the uppermost intercostal arteries began. Three pairs of very large intercostal arteries had almost a common origin from the tapered aorta at this level. The choice at operation was not to sacrifice these intercostal arteries. It was believed that the distal segment below the completely obstructing diaphragm of the coarctation was of sufficient diameter to carry blood distally and that in all likelihood the classic operation of end-to-end anastomosis would be sufficient.

For a few days the child's convalescence was uneventful. He was discharged from the hospital on the eighth postoperative day, but was seen again on the tenth postoperative day because of a cough and fever. Roentgenograms showed what was initially interpreted as fluid in the left side of the chest. Repeated aspirations failed to establish the presence of an empyema or a hemothorax. It was decided that he had atelectasis with secondary pneumonia. On therapy with antibiotics the clinical course and roentgenograms showed sufficient improvement to allow him to return within a few days to his home nearly 300 miles away.

Reports during the next two months indicated a slow recovery in the judgement of his family and the family physician. By September 1956, however, it was quite evident to all concerned that he was not doing as well as could be desired. He returned to Seattle where x-ray films again showed atelectasis of the left lung; in this instance, bronchoscopy demonstrated extrinsic pressure on the left main bronchus with pulsation at the level of the obstruction. Thoracotomy confirmed the presence of a large aneurysm [4] commencing distal to the suture line, and involving the thinned distal aortic segment and extending downward into the aorta around the roots of the first three large pairs of intercostal arteries. Bronchial compression had resulted. Efforts to secure control of the aorta above and below the aneurysm and to control the dilated intercostal arteries were unsuccessful. Massive hemorrhage with cardiac arrest and death occurred during surgery.

Grafts of materials stronger than the patients' own atrophic aortic segments would have resulted in a cure, or at least in eliminating early mortality in these two cases. There proved to be too much temptation to employ vessels which were of adequate diameter without consideration of an obvious lack of strength in the vessel walls themselves.

The third patient's history was sufficiently

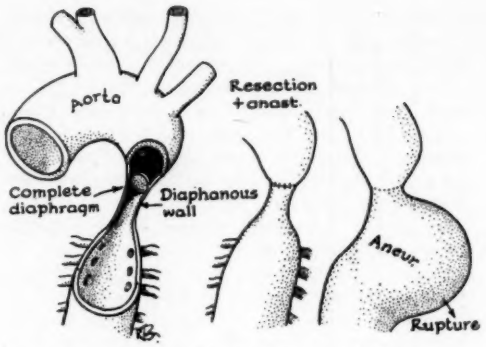

FIG. 3. Coarctation with diaphragm and thin segment which subsequently ruptured.

atypical to indicate the need for very precise preoperative determination of her pathologic condition and for a considerable modification in the approach to the operation.

The diagnosis of coarctation of the aorta in a twenty-three year old woman apparently was made for the first time during a physical examination performed in an emergency ward following a relatively minor automobile accident. It was noted that the blood pressure in her two upper extremities was 180/110 mm. Hg. The femoral pulses were barely discernible. The pressures in her thighs, using a cuff, were found to be only 80 mm. Hg. systolic. Her parents had known that she had had a heart murmur ever since infancy and that x-ray films of her chest taken in early childhood and periodically thereafter showed a shadow in the mediastinum superiorly on the left. Their impression of the reports from her physicians was that she might have tuberculosis or a "tumor." The patient had been cautioned not to participate in gymnastics, but she never had been completely studied to determine a single, logical explanation for these signs.

Accurate delineation of every feature of her problem was of the greatest importance. An initial retrograde aortogram via the brachial artery on the right side did not give a satisfactory outline of the coarctation. An angiocardiogram employing Hypaque,* a 90 per cent contrast medium, was a great deal more successful, however, in that even after passage through both the right and left sides of the heart and the pulmonary circuit the contrast outlined the coarctation very clearly and showed a large aneurysmal dilatation [5] of the upper aorta immediately distal to the narrowed segment. Collateral circulation appeared to be very meager.

The necessity for an extensive aortic resection plus the likelihood of poor collateral circulation recommended employment of hypothermia. Thora-

cotomy was performed after the patient had been cooled to 30°c. Incision in the chest wall confirmed the relative paucity of collateral arteries which almost always mark coarctations. There was a large, extremely thin-walled aneurysm which appeared to have two lobes, as it were. Several intercostal arteries originated from the dilated aorta and had to be sacrificed. The aorta was clamped for thirty-seven minutes so that a prosthesis of dacron and teflon might be employed to replace the excised aneurysmal sac. Within the specimen there were two incomplete diaphragms, but no really narrow obstruction. The diameter at its smallest point was in excess of 1.5 cm. This probably accounted for the poor development of collateral arteries. The patient's postoperative course has been entirely satisfactory from a surgical point of view. The blood pressure in her arms ranges at the time of this writing between 100 and 110 mm. Hg. There are pulsations in the vessels at her ankles.

COMMENTS

These cases illustrate the necessity for caution in evaluating the materials available for restoration of aortic continuity. Sometimes the patients' own tissues are less desirable than foreign material, for example, homografts or synthetics. There is probably no way other than an evaluation by one's physical senses to decide whether the patients' own tissues will be strong enough to endure the new dynamics. The final case shows how a low threshold of suspicion, when findings are atypical, allows one to amplify the usual diagnostic measures in order to plan for anesthesia and operative technics to secure a successful outcome.

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DISCUSSION

John D. Stenstrom (Victoria, B. C.): I fully agree with Dr. Crystal and his coworkers in their contention that the basic operation for coarctation of the aorta should be performed whenever feasible. Associated patent ductus (four in his series, and generally reported to be present in 10 per cent of cases), presents no obstacle to the standard procedure.

I also agree with Dr. Crystal and his associates that until further experience has been gained, grafts, either homologous or synthetic, should not be used in coarctation unless it is absolutely impossible to anastomose the patients own vessels. Even if the lumen of the distal segment is smaller than a graft would be, it is still preferable. It is recognized, however, that further clinical experience may justify an increased use of grafts.

They have demonstrated in the first two cases that arterial and aortic hypoplasia may be and probably is an indication for grafting even if the lumen of the hypoplastic vessel is adequate. It has been proved that a long segment of aorta may be removed and the defect bridged with immediate good results. These grafts have yet to meet the practical test of long follow-up or to answer fully the theoretical objection that they may be weaker in later life than the host aorta. The eventual fate of these grafts in the thoracic aorta is of great interest to all vascular surgeons.

In a significant number of cases, probably about 8 per cent, aneurysms occur in the vicinity of the coarctation arising either from the aorta itself or from the point of origin of the dilated intercostal and bronchial arteries. In order to remove the constriction along with the secondary aneurysm grafting is mandatory. Dr. Crystal, in his third case, did this. In addition, he very wisely cooled the patient and obtained an excellent result. He is to be commended on his foresight regarding the paucity of collaterals.

In summary I would like to thank Dr. Crystal for presenting these cases and for the privilege of commenting upon them. The final chapter on grafts has yet to be written and it is in young people with coarctation whose life span postoperatively should be long that the answer may be found.

William P. Longmire, Jr. (Los Angeles, Calif.): We have recently had a case which I think is sufficiently unusual for presentation.

The patient was a twenty-two year old girl in whom hypertension with severe headaches and occasional convulsions suddenly developed about six months before she was seen. An attempt was made in a hospital in New York to perform an arteriogram through a femoral artery. This was said to have been unsuccessful but indicated that there was some evidence of circulatory insufficiency to the left kidney.

Thinking that the hypertension might have a renal basis the kidney was explored and removed. The hypertension persisted. She was seen by Dr.

Kattus, who believed that she had certain of the signs of a coarctation.

At exploration we found a typical area of coarctation without any indentation, but it was occupied by a hard, firm mass. The pleura was opened and the vessel exposed. Clamps were placed above and below the site of the suspected coarctation. Incidentally, this patient was also under hyperthermia.

On opening the area, however, it was apparent that rather than a coarctation there was an intra-aortic tumor. The region of the aorta below this point also felt thickened. It was our first impression that this probably represented a thrombosis, but then it became apparent that the tumor extended down into the aorta.

The tumor could be freed from the wall of the aorta with ease. The tumor was elevated. At that point the tumor was attached to the intima and media of the aorta just opposite the take-off of the left subclavian artery.

In the proximal portion of the aorta, one clamp was placed on the subclavian artery and another clamp on the proximal part of the aorta. The tumor arose from the edge of the intima which had been incised.

We performed lower arteriotomy after mobilizing the entire thoracic aorta, placing clamps on the intercostal vessels, but again we were unable to free this tumor.

There were two openings in the aorta and the tumor completely filled the aorta. Finally the lower clamp was removed. A long curved clamp was placed down into the abdominal aorta. Tugging on the tumor, we were able to dislodge an entire cast of the complete aorta with extension down into the iliac arteries, and the tumor ended in a blind end. It was not broken off but came entirely free.

The tumor branched into the celiac and superior mesenteric arteries and into the renal arteries. This, of course, was interfering with the blood supply to the kidneys not only because of the complete obstruction of the aorta at this point, but because of the extension of this tumor tissue into the renal artery.

Upon removal of the tumor the patient's blood pressure fell from 240 to 120 mm. Hg. Over the next four or five days it came back to around 160 mm. Hg at which it remains at this time. The patient is asymptomatic.

The tumor was a myxofibroma, the malignancy of which has not, at this time, been determined. I think it is probably of low grade malignancy but obviously has grown very slowly over a long period of time.

DAVID J. DUGAN (Oakland, Calif.): I would like to call attention to an unusual type of coarctation-like anomaly discovered unexpectedly in a patient who presented no particular signs of coarctation. This was a four year old child whose case was reported in the *Journal of Thoracic Surgery* about a year and a half ago. She presented with the signs of cyanosis of the lower extremities. There were normal blood pressure determinations in both the upper and lower extremities. The child was debilitated and in a generally rundown condition.

The child underwent the usual catheterization studies, which I must confess were not particularly helpful. She was explored on the basis of the increased pulmonary arterial pressure and the cyanosis in her lower extremities. On the left we found a rather unusual situation with an absence of the aortic isthmus. The aorta was normal in its take-off from the base of the heart. However, it extended into a rather large and dilated left subclavian artery. There was no descending arch of the aorta or normal arch. However, there was a normal but rather large left main pulmonary artery with a very large left pulmonary branch which made up the descending aorta.

The patient had enough circulation to the left lung to adequately handle the situation, and by clamping this, what might be called an oversized ductus, it was found compatible with normal existence. Anastomosis was performed between this descending left pulmonary arterial branch to the base of the subclavian artery. The patient has done well. The cyanosis has disappeared from the lower extremities. However, she has a systolic murmur which has been reinvestigated recently, showing an interventricular structural defect which will be repaired in the near future.

We have found it very convenient to observe this girl inasmuch as she happens to be a classmate of my child.

K. ALVIN MERENDINO (Seattle, Wash.): I would like to point out that in keeping with the message of our President, it is important to have individuals in our Surgical Society who have special interests. Certainly, as general surgery moves ahead, those in the specialties are moving ahead as well, forming a body of knowledge which is important to general surgery. However, because of poor liaison, we as general surgeons do not have ready access to it.

We have had a very unhappy circumstance in which we had utilized the left subclavian artery as the arterial input for an open heart perfusion. At autopsy, we found that we had ligated the dominant vertebral artery, which resulted in damage to the mid-brain and death. We then analyzed seventy adult brains and also twenty infant brains. Actually, our findings are similar to those in the literature, in which there is considerable information that is well-known to the neurosurgeons; viz., that the left vertebral artery is the dominant vertebral artery, and also if one ligates either vertebral artery, the possibility of death caused by damage to the mid-brain is very real, due to absence or inadequate

communications with the basilar artery of the opposite vertebral artery.

I would like to point out that when the left subclavian artery is used for arterial input in extracorporeal bypass, and the left vertebral artery is sacrificed, the incidence of death due to injury to the mid-brain will be 3.1 per cent. Also, when one sacrifices the right vertebral artery, the incidence of death due to disturbances in the mid-brain is approximately 2 per cent. In these situations, the opposite vertebral artery for all intents and purposes is absent. This, however, takes no cognizance of the fact that additional studies show that the left vertebral artery is twice as big as the right in 9 per cent of the patients, and the right vertebral artery is twice as large as the left in 5 per cent of the cases. What the death rate might be when both vertebral arteries are present and the dominant one is ligated is unknown. Therefore, certainly when one ligates a vertebral artery, the minimal death rate is predictable.

The importance of these anatomic variations has implications other than in open heart surgery: for example, in operative procedures such as the Blalock-Taussig operation for tetralogy, one vertebral artery is often sacrificed when the subclavian artery is mobilized; and in certain cases of coarctation, also, when the subclavian artery may be permanently or temporarily occluded, and vertebral flow must of necessity be retrograde, damage to the mid-brain, with death of the patient, will occur in a predictable percentage of cases, dependent upon the fixed incidence of anomalous basilar-vertebral arterial communications. Thus, in operations for coarctation, one should avoid when possible the simultaneous occlusion of the proximal aorta and left subclavian artery. Where the proximal cuff is short, the proximal clamp should be placed tangentially in such a fashion to allow flow, although reduced, into the left subclavian artery for perfusion into the left vertebral artery. Otherwise, the possibility exists that a successful technical operation may result in death of the patient.

DEAN K. CRYSTAL (closing): First of all I want to thank all the discussers. Dr. Stenstrom was considerably less harsh than he might have been, it seems to me, in evaluating our failures. I thought we learned pretty slowly.

I think nobody can make adequate comment about that case of Dr. Longmire's. We all commend him, and every one who is interested in these things is envious and would like to have seen a case like it.

I think Drs. Dugan and Samson found a better solution to their problem than we did in ours in which we had an absent aortic arch. I will point out that they may have been a little more fortunate, because the section of the pulmonary artery they used evidently was equal to the pounding which a vessel gets when it is attached close to the center of things, as it were.

I am particularly pleased that Dr. Merendino took this opportunity to discuss abnormalities of the subclavian artery because I know of the work which he and his group have done relative to the vertebral artery and I believe that it does have an application to open and closed cardiovascular procedures. In the very small experience with open heart technics we, too, have come to believe that the subclavian artery is not a good point for perfusion.

Acute Inferior Mesenteric Vascular Occlusion, a Surgical Syndrome

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WHILE acute inferior mesenteric vascular occlusion is generally a lethal disease, it usually produces a clinical picture which may be diagnosed and successfully treated. Occlusion of the inferior mesenteric vessels has seldom been thought of as a separate clinical entity [*5,17*]. Most discussions of mesenteric vascular occlusion are based almost entirely on involvement of the superior mesenteric artery, which is affected in more than 90 per cent of cases [*12*]. Acute occlusion of the inferior mesenteric vessels accounts for about 2 to 3 per cent of cases of mesenteric infarction [*1*].

A review of the literature on mesenteric occlusion in general reveals that Tiedeman in 1843 reported the first known case and Virchow in 1847 described the salient pathologic features of this condition. In 1895, Elliot performed the first successful resection for this disease, and in 1954 Uricchio et al. [*20*] were able to find only 158 survivals after bowel resection. Significant contributions to the general subject of mesenteric vascular occlusion have been made by Jackson, Porter and Quinby [*7*] (214 cases) in 1904, Trotter [*19*] (360 cases) in 1913, Loop [*11*] (500 cases) in 1921, Cokkinis [*3*] (76 cases) in 1926, Meyer [*15*] (92 cases) in 1931, and Brown [*2*] (772 cases) in 1940. Excellent reviews of this subject have appeared recently [*6,8*].

This is a review of fourteen verified cases of acute inferior mesenteric vascular occlusion as seen at the Los Angeles County Hospital during the last eight years. There were eleven men and three women in this series; the age range was fifty-nine to eighty-five, with an average age of sixty-five. In this study emphasis is placed on early diagnostic clinical findings and the distinctive features of infarction of the descending colon.

ETIOLOGY

The predominant cause of the mesenteric infarction in this series was arterial thrombosis, which was present in eleven of the fourteen patients or 78.6 per cent. Venous thrombosis accounted for two cases or 14.3 per cent, and both arterial and venous thrombosis appeared likely in one patient. Serious concomitant conditions were present in most instances, with cardiovascular disease and various malignancies being most common. Thrombosis of the inferior mesenteric artery arising from a saccular aortic aneurysm occurred in two cases. The inferior mesenteric vessels were selectively involved in all fourteen patients. All were verified by either operative findings or postmortem examination, and all had hemorrhagic infarcts.

Mesenteric occlusion after surgery for unrelated conditions developed in four patients (Table 1), and others have reported this associa-

TABLE 1
POSTOPERATIVE INFERIOR MESENTERIC INFARCTION

Surgical Procedure	Time of Onset after Operation (days)	Type of Occlusion and Extent of Infarction
Hemorrhoidectomy.....	4	Arterial thrombosis, perforated and gangrenous descending colon
Vagotomy-pyloroplasty...	7	Venous thrombosis, hemorrhagic infarction splenic flexure to rectum
Ureterosigmoidostomy and sigmoid colostomy	10	Arterial thrombosis, gangrenous descending and sigmoid colon
Above knee amputation..	14	Arterial thrombosis secondary to saddle aortic embolus, gangrenous sigmoid colon and rectum

tion in as high as 30 to 40 per cent of their cases [9,18]. Thrombotic occlusions may be precipitated by operative trauma, blood dyscrasias, atheromatous plaques, saccular aortic aneurysm, aortography, sepsis and after splenectomy.

CLINICAL FEATURES

The most striking feature of acute mesenteric infarction is sudden, severe abdominal pain out of proportion to the physical findings. Acute abdominal pain was prominent in all patients in this series. Sudden occlusion of the inferior mesenteric vessels tends to produce lower abdominal pain and tenderness in contrast to the upper or more generalized abdominal pain and tenderness of the superior mesenteric type. Dunphy and Zollinger [4] believe this pain is due to anoxemia of the intestinal musculature and is a true visceral pain conducted by the sympathetic nervous system.

Localized tenderness and rigidity in the left lower quadrant are present early in infarction of the descending colon from occlusion of the inferior mesenteric vessels, but findings may later be generalized if perforation of the colon occurs.

A bloody rectal discharge is a prominent feature of infarction of the descending colon. It was present in thirteen of fourteen patients or in 92.3 per cent of this series. Blood is extravasated into the intestinal wall, lumen, mesentery and peritoneal cavity, and bloody stools are almost always present with occlusion of the inferior mesenteric vessels. Litten in 1880 observed that tenesmus accompanied by bright red stools should suggest this diagnosis.

Shock may develop as intestinal infarction progresses, and its severity usually parallels the extent of bowel involvement. Some degree of shock was present in the majority of patients. Venous obstruction intensifies the shock, resulting in massive sequestration of blood and fluid into the bowel and peritoneal cavity which may produce death before gangrene develops. Shock appearing later may be due to peritonitis.

It is unusual to have distinctive x-ray findings in mesenteric infarction. Early leukocytosis is the only constant laboratory finding, and this rises with progression of tissue necrosis and peritonitis.

Bloody fluid obtained by peritoneal aspiration is a helpful finding in mesenteric infarction, even though it may also be present in other acute abdominal conditions.

Sigmoidoscopic demonstration of ischemic changes of the rectosigmoid mucosa strongly suggests the presence of inferior mesenteric vascular occlusion. At sigmoidoscopy the mucosa appears bluish black and is accompanied by a bloody putrid discharge. This finding was observed in the last three patients in this series. Experimental studies have shown that intestinal mucosa is particularly susceptible to ischemic change [10], making it probable that vascular insufficiency would appear first in the mucosa. Therefore the sigmoidoscopic findings should appear early.

TREATMENT

Seven of the fourteen patients were explored surgically, but only four of these received any definitive treatment. The only successful case was treated by wide obstructive resection of the descending colon. Two other patients were also treated in a similar manner. One underwent a simple exteriorization procedure. The mortality rate for this series was 92 per cent.

The first step in treatment is vigorous blood replacement, concomitant antibiotics, and early surgery with wide obstructive resection of the descending colon. This procedure consists of resection of the descending colon from the mid-transverse colon to a viable area of sigmoid or rectosigmoid. If a viable portion of rectosigmoid cannot be brought out as a mucous fistula, it may be closed and left in an extraperitoneal position with drainage. Later, if the patient's condition permits, intestinal continuity may be re-established by dismantling the transverse colostomy with reanastomosis to the rectosigmoid. If necessary, the patient may be left with a permanent colostomy.

Anticoagulants, particularly heparin, have been advocated in the treatment of this disease in order to minimize thrombotic propagation. Serious associated conditions should be corrected prior to operation if possible.

The direct operative approach has been successfully applied to occlusive disease of the superior mesenteric artery, but the inferior mesenteric artery seems less adaptable to such procedures because of its smaller size and infrequent involvement by emboli.

The mortality in mesenteric vascular occlusion remains high because of delay in diagnosis, the extensive involvement of gangrenous bowel and the serious associated diseases. The only factor which it is possible to influence sig-

nificantly is the delay in diagnosis. The correct diagnosis in this series was made in only four of the fourteen cases. The use of diagnostic sigmoidoscopy should make earlier recognition possible. Prompt recognition, vigorous blood replacement and early aggressive surgery provide the only opportunity for reducing the high mortality.

CASE REPORTS

The clinical picture of acute severe pain in the left lower part of the abdomen usually accompanied by blood in the stool and the demonstration of ischemic mucosal changes by sigmoidoscopy is illustrated by the following two case reports.

CASE I. E. S., a sixty-eight year old white man, was admitted to the Los Angeles County Hospital on January 30, 1958, with a two-day history of sudden pain in the left lower part of the abdomen. The pain became increasingly severe, was associated with tenesmus, and the passage of bloody stools. On physical examination the patient was acutely ill with cold extremities consistent with incipient shock. He complained of excruciating pain in the lower part of the abdomen. The temperature was 101°F., the pulse was 120, and the blood pressure was 144/76 mm. Hg. The lower part of the abdomen was markedly tender and rigid, with signs of diffuse peritonitis. Gross blood was noted on rectal examination, and on sigmoidoscopy there were bluish black areas of mucosal gangrene in the rectosigmoid area. A diagnosis of inferior mesenteric vascular occlusion was made, and the patient was prepared for surgery with blood, plasma, antibiotics and digitalization. At surgery there were patchy areas of greenish black gangrene of the entire descending colon including the extraperitoneal part of the rectum. Wide obstructive resection of the descending colon was performed, the distal part of the rectum oversewn, and closed extraperitoneally and drained. Two small polythene catheters were inserted into the pelvis for a 1 per cent neomycin solution to be irrigated at frequent intervals. After surgery the right transverse colostomy remained viable and functional, and the patient's recovery was uneventful. Three months later the transverse colon was anastamosed to the rectum, re-establishing intestinal continuity. Two weeks later he was discharged from the hospital after a satisfactory convalescence.

CASE II. H. S., a seventy-two year old Caucasian man, was admitted to the Los Angeles County Hospital on November 21, 1957, in a state of mental confusion. Relatives stated that he had been complaining of severe abdominal pain for three days. There was no vomiting. The patient had been treated for years for arteriosclerotic heart disease with heart block and congestive failure had developed in the month preceding admission. On physical examination, he was in a shock-like state, with a tachycardia of 120, and was lying in a pool of bloody stool. The heart rate was regular, and the blood pressure was 110/70 mm. Hg. The abdomen was slightly distended with generalized tenderness and rigidity. There were no abdominal scars or palpable hernial masses. Dark red blood was found in the rectal ampulla, and there was an exquisitely tender, cystic mass in the cul-de-sac. Sigmoidoscopy showed mucosal necrosis at the 6 inch level, with mottling, cyanosis and superficial ulceration. Laboratory findings included: hemoglobin, 16.5 gm. per cent; white blood count, 20,600 per cu. mm. with 81 per cent polymorphonuclear leukocytes; blood urea nitrogen, 108 mm. Hg; and a normal serum amylase. Abdominal x-ray films showed no evidence of distention of the small or large bowels. Abdominal paracentesis produced a small amount of putrid, serosanguineous fluid. A diagnosis was made of occlusion of the inferior mesenteric vessels with infarction of the descending colon, and the patient was prepared for surgery with antibiotics, blood and plasma. At surgery the entire descending colon was found to be gangrenous with fresh thrombus occluding the inferior mesenteric artery. Left colectomy was performed with establishment of a distal mucous fistula and the transverse colon was brought out as a colostomy. Profound shock developed in the patient shortly after the surgical procedure was started, and there were noted abnormal neurologic signs including pupillary inequality and a positive Babinski sign. Tracheostomy was performed immediately after closure of the abdomen, but the patient died before he could be removed from the operating table. No autopsy was obtained.

COMMENTS

While arterial occlusion due to either embolism or thrombosis is usually more fulminating than venous thrombosis, this clinical distinction is rarely possible. There are two general clinical types of acute mesenteric occlusive disease: sudden, complete occlusion of a major mesenteric artery, or gradual occlusion of an artery or vein. When massive intestinal infarction with gangrene results, the clinical picture is about the same no matter how it started. Severity of the symptoms depends more on the size of the occluded vessel and extent of infarction than on the type of occlusion. Trotter observed that perforation of the bowel is more apt to occur when the inferior mesenteric vessels are occluded, and he attributed this to the thinner

TABLE II
COMPARATIVE FEATURES

Data	Superior Mesenteric Vascular Occlusion	Inferior Mesenteric Vascular Occlusion
Frequent etiology	Embolism	Thrombosis
Location of pain	Mid-abdomen	Left lower quadrant
Collateral circulation	Poor	Abundant
Blood in stool	Inconstant	Very frequent
Gangrene	Constant	Less likely
Sigmoidoscopy	.....	Diagnostic value

intestinal wall and more infective fecal content of the colon.

Gradual obliteration of the mesenteric arteries may allow collateral circulation to develop and prevent actual necrosis of the bowel. Intestinal ischemia resulting from mesenteric arterial obstruction may present a recognizable syndrome and has been aptly termed "intestinal angina [*16*]." Intestinal gangrene is less frequent following occlusion of the inferior mesenteric vessels than it is when superior mesenteric vessels are involved. The area of the descending colon is protected by an adequate collateral circulation through the middle colic artery via the marginal artery of Drummond above, and through the middle and inferior hemorrhoidal arteries below. Infarction of the descending colon is rarely abrupt and tends to be patchy. These pathological changes may be explained by the minimal intramural circulation at the antimesenteric border. The infrequency of ischemic necrosis of the descending colon following ligation of the inferior mesenteric artery demonstrates the usual effectiveness of the marginal arteries of the collateral circulation [*13*]. Hemorrhagic infarction with gangrene almost always follows sudden closure of the superior mesenteric artery. The superior mesenteric artery is of large caliber, about 9 mm. in diameter, and runs parallel with the aorta. For these reasons it is a trap for emboli. The inferior mesenteric artery is half this size, takes off from the aorta at a greater angle and is rarely involved by an embolus. The contrasting features of the superior and inferior mesenteric occlusions are shown in Table II.

SUMMARY

1. Fourteen cases of inferior mesenteric vascular occlusion have been presented. One patient was successfully treated by wide obstructive resection of the descending colon. The over-all mortality was 92 per cent.

2. Acute inferior mesenteric vascular occlusion has distinctive clinical features consisting of sudden, severe pain in the left lower part of the abdomen, usually accompanied by blood in the stool. Shock is a frequent early finding.

3. The demonstration of ischemic mucosal changes by sigmoidoscopy facilitates early diagnosis.

4. The reduction of mortality in mesenteric vascular occlusion depends upon earlier diagnosis and prompt, aggressive surgical treatment.

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DISCUSSION

LEON GOLDMAN (San Francisco, Calif.): It is timely that the authors have called to our attention the serious syndrome of mesenteric vascular occlusion, for with increasing longevity this problem arises more frequently, and present day advances in vascular surgery may potentiate certain improvements in surgical therapy in the future.

Early diagnosis is mandatory if we are to reduce the frightful mortality rate and prevent the need for subtotal enterectomy when the superior mesenteric artery is involved, a surgical sequella which is incompatible with life. We must think more and more of the possibility of abdominal symptoms being produced by obliterative vascular disease in elderly patients, particularly when they have other manifestations of arterial disease. Clinical differentiation between superior and inferior mesenteric occlusion is not always possible or necessary.

The inferior mesenteric artery was ligated at its origin in over 120 operations on the abdominal aorta with only one instance of ischemia of the descending colon. This exception occurred in a patient with an aneurysm of the abdominal aorta and thrombosis of both hypogastric arteries, requiring resection of the descending colon to the pelvic floor at the same operation. This confirms the authors' statement that there must be additional arterial occlusion to that presented in the inferior mesenteric artery itself. Reports and experience indicate that a history of previous attacks preceding the fatal one by weeks, months or years can be elicited in the majority of patients. We agree with the authors that the pain, degree of shock and rapid deterioration of the patient usually overshadow the abdominal findings. The severity and persistence of pain and this paucity of abdominal signs may be the most significant clinical manifestations of this catastrophe, in the early stages.

Resection in cases of inferior mesenteric arterial occlusion is necessary; with the extensive resection required in superior mesenteric arterial block such a short segment of bowel is left that the patient succumbs to malnutrition.

If we can but make the diagnosis during the reversible stage of ischemia, then endarterectomy, by-pass or implantation of the patent portion of superior mesenteric artery into the aorta may prove life saving.

A patient with inferior mesenteric arterial occlusion entered the hospital ten days after the onset of pain, vomiting and black diarrheal stools. He had had bilateral supracondylar amputations for arteriosclerotic gangrene two years previously. The barium enema showed a ragged outline of what was taken to be the descending colon. At autopsy following a right-sided transverse colostomy there was a thrombosis of the inferior mesenteric artery and obliteration of the hypogastric arteries with complete necrosis of the descending and pelvic colon, walled off from the free peritoneal cavity, so that the patient was still passing liquid stool through this walled off channel.

The Macroscopically Non-pathologic Gallbladder

GORDON F. MADDING, M.D., *Burlingame, California*

THE majority of gallbladders removed contain stones which may or may not produce symptoms. When symptoms are present the patient is improved in 90 to 95 per cent of cases by cholecystectomy. When there is gross disease of the gallbladder without evident stones, its removal is attended by relief of symptoms in a slightly smaller percentage of cases. The care of the third type of gallbladder, encountered on rare occasions, which has previously been diagnosed as chronic cholecystitis but which at the time of surgery shows none or only minimal evidence of disease, is the problem to be discussed. At least 90 per cent of biliary tract disease is associated with calculi but in most reported series 4 to 6 per cent of all gallbladders removed are both non-acute and acalculous. That such a problem exists has been clearly stated by Snell [20] who writes: "It is well recognized that all symptoms of cholecystic disease including those closely resembling colic may be present without much visible evidence of either infection or cholesterosis; yet removal of the gallbladder not infrequently will relieve the presenting symptoms." The problem of determining whether removal of the gallbladder is in the best interests of the patient when the condition is discovered at operation prompted this study.

TABLE 1
CHOLECYSTECTOMY (1948–1956)

Year	No. of Cholecystectomies	No. of Non-acute Alcalculous Gallbladders	Per cent
1948	68	5	7.3
1949	48	2	4.2
1950	64	6	9.3
1951	74	5	6.7
1952	79	4	5.0
1953	89	5	5.6
1954	75	6	8.0
1955	70	2	2.8
Totals..	567	35	6.1

This is a controversial subject and at the outset the problem to be discussed should be clarified. The macroscopically non-pathologic gallbladder is not synonymous with the normal gallbladder. The gallbladder to be considered is abnormal as determined by symptoms, repeat cholecystograms revealing impaired or absent function, and histologic examination in most cases.

Colcock and McManus [1] reported that 4.2 per cent of the gallbladders removed at the Lahey Clinic from 1950 to 1953 were non-acute and acalculous. Glenn and Mannix [2] reported a series of 135 patients on whom their group had performed cholecystectomies for non-calculous conditions of the gallbladder not acutely involved. The 135 patients in their series represent 4.3 per cent of all patients treated surgically on the pavilions of The New York Hospital for chronic biliary tract disease during a twenty-two-year period. My study represents an eight-year survey (1948 to 1956) conducted at a local private hospital, during which period thirty-five cholecystectomies were performed by fifteen surgeons for non-acute acalculous gallbladders. (Table 1.)

Cases in which cholecystectomy was performed following previous cholecystostomy have been excluded. All patients in whom stones were absent in the gallbladder but present in the common duct have been excluded, as well as those on whom cholecystectomy was performed during the course of sphincterotomy. In this group of thirty-five patients there were eleven males (31.4 per cent) and twenty-four

females (68.6 per cent). The average age was forty-eight and seven-tenths years.

Without exception, the clinical history as recorded was compatible with disease involving the gastrointestinal tract. In less than half the patients a history of biliary colic was obtained, and in others the symptoms were non-specific and could have been caused by biliary tract or other intra-abdominal conditions.

Physical examination was helpful in approximately 40 per cent of the group in whom tenderness was elicited in the right upper quadrant of the abdomen over the area of the gallbladder.

Oral cholecystograms were taken in twenty-five patients (71 per cent of the group). Not all the roentgenographic studies were made in the hospital where surgery was performed. Of these, twenty-three (85 per cent) revealed pathologic function of the gallbladder. In some the radiologic description varied from no filling or poor filling to faintly visualized. In others the statement was made that it was impossible to exclude the presence or absence of calculi.

OPERATIVE FINDINGS

The surgeons' operative notes revealed what they considered to be evidence of disease of the gallbladder in 92 per cent of the cases. In this group the pathology described varied from a gallbladder distorted by adhesions or involved by thickening or scarring to one having an abnormal cystic duct.

PATHOLOGY

On histologic examination six of the gallbladders removed were non-pathologic; two of these were described as having abnormal cystic ducts. Eighteen showed chronic cholecystitis in varying degrees, and in eleven a diagnosis of cholesterolosis was made. (Table II.) The cystic duct was specifically mentioned in four cases. In one it was described as narrow, and in another the mucosal folds were felt to be enlarged in the distal portion of the gallbladder and could have periodically occluded the cystic duct opening. In two there was a papillary infolding of the cystic duct mucosa.

In the group of thirty-five patients, twenty-seven have been followed up for a period of one and a half to eight years. This follow-up period is short and perhaps not long enough for symptoms to become apparent if they are to occur as a result of removing such a gallbladder. In the entire group there was one death due to an unrelated disease, and one patient required further surgery a year later for the removal of a common duct stone.

TABLE II
PATHOLOGIC HISTORY

Histology	No. of Cases	Per cent
Normal	6	17.2
Chronic cholecystitis	18	51.4
Cholesterolosis with or without chronic cholecystitis	11	31.4
Totals	35	100

Complications noted in this group were two cases of wound dehiscence requiring secondary closure and one case of massive atelectasis. There were no hospital deaths and all patients were discharged in good condition.

COMMENTS

The material for the conclusions presented herein was obtained from three sources: (1) a review of the literature dealing with this problem; (2) correspondence with a number of authorities in this country obtaining their opinions regarding this problem; and (3) information derived from the study I conducted at a local private hospital. It is fully realized how difficult it is to evaluate clinical problems statistically, particularly from a series as small as the one I studied but the results in this group were essentially the same as those from institutions reporting larger series.

Twenty-seven patients have been observed for a period of one and a half to eight years and good results (cured or improved) were found to follow in 70.3 per cent. There were no immediate postoperative deaths. The immediate morbidity in this group was not significantly greater than that seen in a comparable series of cases in which calculi were present. The results in the six patients having pathologic reports of normal gallbladders is of interest. One was lost to follow-up, one was classed as a poor result and four were regarded as good results. The fact that 70 to 75 per cent of patients in most reported series (Table III) as well as in my study

TABLE III

Author	Year of Study	Cured or (%) Improved
Mackey	1934	58.4
Schafer	1936	74.0
Doehring	1940	76.2
Glenn	1956	76.0
Present study	1957	70.3

obtained good results demonstrates that biliary symptoms can be relieved in the majority of cases by removing the macroscopically non-pathologic gallbladder when it is discovered under the circumstances discussed.

What then should we do when confronted with a patient in whom a pathologic gallbladder was thought to exist from the history and laboratory findings, including evidence of impaired function by at least two cholecystographic studies, and in whom full studies have been made to exclude other pathology, but which on gross examination at the time of surgery appears to be uninvolved or only mildly so?

A thorough search should be made to demonstrate disease of the gallbladder and in the absence of this all abdominal organs, particularly those adjacent to the gallbladder, should be evaluated in an effort to exclude pathology which might be responsible for the symptoms. Babcock and Eyerly [3] found that 1.4 per cent of their 1,055 patients explored for gallbladder disease had other conditions, not of the biliary tract, urgently in need of surgery. The limitations of physical examination in defining disease of the gallbladder must also be appreciated. In Glenn's series of 135 patients, more often than not the surgical pathologist believed the gallbladder removed to be within the limits of normal or to have only minimal changes. On microscopic examination, however, evidence of chronic cholecystitis was reported in 100 cases (74 per cent).

Emptying of the gallbladder by needle aspiration will aid in our ability to palpate small stones, polyps or thickening due to cholesterolosis. In addition, examination of the aspirated bile can provide helpful information. An operative cholangiogram performed transvesically may be helpful in defining any narrowing, tortuosity, stricture, kinking due to a redundant cystic duct or other obstructive factors involving the cystic duct, as well as demonstrating dilation of the common duct secondary to obstruction at the sphincter of Oddi.

Hayes and his associates [19], in a recent clinical study of bile duct anomalies, found a 47.25 per cent incidence of clinically significant deviations from the anatomy hitherto considered normal and so described in anatomic texts. In the light of these findings they raise a question regarding the part these anomalies play in the etiology of non-calculous as well as calculous cholecystitis because of the disturbance in drainage with consequent stasis.

If operative cholangiograms reveal a normal-appearing biliary tree, exploration of the sphincter of Oddi may be considered. Baker [4] noted that fibrosis of the sphincter of Oddi cannot be ruled out by operative cholangiography, for the duct is not always dilated. Stenosis of the sphincter of Oddi is now accepted as a definite entity and one which may produce persistent and severe symptoms in the absence of stones in the common duct or gallbladder. Wangensteen [5] for the past three years has performed common duct exploration during the course of cholecystectomy for gallstones, and in twenty-nine cases (58 per cent) could not pass a No. 3 Bakes dilator without force. He believes such an ampulla is abnormal and can cause biliary stasis which in turn will lead to gallstone formation. This belief is supported by his experimental work which incriminates pancreatic juice activated by bile and gastric juices as possible agents responsible for the narrowing of the sphincter.

It would seem that after carrying out the diagnostic procedures discussed, without discovering biliary pathology, we are left with five possible courses of treatment: (1) close the abdomen without definitive treatment directed at the biliary tract; (2) remove the gallbladder but perform no other surgical procedure; (3) remove the gallbladder and explore the sphincter of Oddi for evidence of obstruction such as spasm or stenosis, and if such is found, perform sphincterotomy; (4) remove the gallbladder and perform sphincterotomy regardless of the findings; and (5) preserve the gallbladder but perform a short-circuiting procedure by anastomosing it to the small intestine.

The first course would seem to be undesirable for we must assume that the clinical and laboratory findings strongly pointed to gallbladder disease and that full studies had been

made preoperatively to exclude other pathology. In addition Glenn found that when the gallbladder was examined by the pathologist there was a considerable error in his ability to diagnose accurately disease of the gallbladder macroscopically. This limitation probably applies to the operating surgeon as well.

I believe the second course is the procedure of choice, for approximately 70 per cent of the patients in this as well as other studies in whom this course was followed obtained satisfactory results. Of the remaining 30 per cent in this study, only one patient required reoperation because of the severity of symptoms; a common duct stone was diagnosed and removed one year later. Even though the gallbladder is not a nuisance organ like the appendix, for it does have functions, these can be dispensed with and not produce symptoms. This is evidenced by the fact that at least nine of ten patients who have a diseased gallbladder removed are comfortable thereafter so far as loss of the gallbladder is concerned.

The third course seems unjustified in view of the results obtained with the second method. The increased mortality and morbidity related to the routine exploration of the sphincter would be too great to justify the additional surgery. We must consider the gallbladder, common duct, sphincter of Oddi and pancreas as a reciprocating group associated with much inter-relationship. It is entirely possible that as we learn more about the sphincter mechanism and its reaction in diseased states, any further improvement we may expect in the therapy of this group will result, in part at least, from the application of the third course. It is in this group in which the gallbladder has been removed for meager findings that most of the dyskinesias will occur [*21*].

The fourth course would be attended by the same disadvantages as the third. Dilatation of the sphincter of Oddi has been used by some as an alternative to performing sphincterotomy. The dilatation and lack of sphincter function which follow this procedure are only temporary. Branch and his co-workers [*6*] have shown that in the dog experimental dilatation of the sphincter of Oddi produces no permanent enlargement and is followed by actual scarring when extensive dilation is carried out. Zollinger [*7*], Cattell [*8*] and Glenn [*9*] also believe that when the sphincter is forcibly dilated an undesirable sequence of events can be expected, and the resulting condition may be worse than the original state.

The fifth course of treatment seems unwise in view of the lack of necessity for maintaining the gallbladder for possible use in a by-pass operation to relieve jaundice resulting from obstruction of the ampulla due to carcinoma of the pancreas or periampullary area. The incidence of carcinoma in this location has been noted in less than one-tenth of 1 per cent of all patients admitted to large general hospitals. Of more importance would be the delay in appearance of jaundice (often the first sign) following obstruction from a carcinoma arising in the aforementioned area were this method used. Thus, such a patient would be denied earlier treatment and possibly any opportunity of cure by resection. Unless the patient's life expectancy is of short duration, cholecystenterostomy is an undesirable procedure, for the stoma tends to become constricted and stenose. The incidence of duodenal ulcer would undoubtedly be greater in this group as well because of the diversion of the alkaline bile from the duodenum.

Regardless of the procedure followed, a liver biopsy should be performed. Further study and the patient's subsequent course may reveal that the symptoms were due to a liver disturbance such as hepatic biliary obstruction of the cholangitic type (from intrahepatic biliary canalicular obstruction from bile pigment due to Thorazine® or methyltestosterone) or from an early cholangitic cirrhosis. If either of these is found, the added information obtained from the liver biopsy will make better treatment possible.

The opinions expressed in the literature by some authors varied regarding the procedure used under these circumstances. Lahey [*10*] has expressed the belief that if symptoms are unrelieved by medical management, the gallbladder should be removed regardless of the findings. Glenn [*2*] states that at The New York Hospital when it is presumed that a patient has cholecystitis with stones and no stones are found, immediate consultation at the operating table is requested. The history is reviewed, local findings are evaluated and a decision is reached concerning cholecystectomy. He [*11*] further states, however, that "repeated cholecystograms that reveal impaired function are an indication for cholecystectomy."

A letter was directed to a number of surgeons

interested in disease of the biliary tract requesting their procedure when such a gallbladder is encountered. Their replies are as follows: Cattell [12] writes that "if the clinical symptoms strongly point to gallbladder disease and full studies have been done preoperatively one is certainly justified in removing the gallbladder if no other pathology is encountered . . . I do not believe that removal of the gallbladder produces gastrointestinal symptoms."

Cole [13] has expressed the following opinion: "The primary error in cholecystography is related to a normal cholecystogram when the gallbladder is the cause of the symptoms and when the symptoms will be obliterated by cholecystectomy. The explanation is not difficult since I am quite sure that disease of the cystic duct is present which produces a partial block, but has not yet produced cholecystitis or cholelithiasis. If a patient has definite symptoms of gallbladder disease, including severe pain in the right upper quadrant I am willing to condemn the gallbladder even though it appears normal at the operating table and concentrates the gallbladder media quite well . . . I have done this on numerous occasions and almost invariably symptoms have been relieved . . . I am quite convinced that removal of a normal gallbladder produces no postoperative gastrointestinal symptoms . . . if the common duct were not dilated I doubt very much I would open it to explore the sphincter of Oddi even though I was removing the gallbladder, the dome of which appeared relatively normal. If there has been a history of jaundice or other indications for opening the common duct are present then one has ample justification for testing the patency of the sphincter of Oddi. It is my rule that if a 6 mm. scoop goes through the sphincter readily it is probably not diseased, on the contrary if it does not go through I open the duodenum and actually look at the sphincter. I cut it whenever there is an obstruction according to the criteria mentioned above."

Crile [14] also believes that removing a normal gallbladder as the only surgical procedure is not productive of postoperative gastrointestinal symptoms. He further writes that although it is rare to be presented with a patient having what appears to be a pathologic condition of the gallbladder clinically yet who at the time of surgery is found to have no gross disease of the biliary tract, this is occasionally encountered with cholesterolosis of the gallbladder when it can be removed and the patient benefited. Such pathologic findings were present in one-third of this series.

Dorsey [15] writes, "If all other reasonable testing is negative and there are recurrent localized findings pointing to the biliary tract even though cholecystography reports a normally functioning gallbladder, laparotomy with the intention of doing cholecystectomy is warranted with the patient's complete knowledge of the state of affairs."

Coller [16] has stated that he would remove the gallbladder under the circumstances being discussed if the patient had experienced severe colicky pain in the right upper quadrant, an episode of which he had witnessed.

Doubilet [17] has written, "If after opening the abdomen you are unable to find any pathologic disorder and feel impelled to remove the gallbladder, you should perform sphincterotomy."

Walters [18] writes, "If I am uncertain as to whether there is disease in the gallbladder and the patient has a good clinical history of biliary tract disease, I perform cholecystectomy, but not sphincterotomy."

SUMMARY AND CONCLUSIONS

Discussion of the non-acute acalculous gallbladder is a sound subject for any group of surgeons to consider, for I am sure that all have had experience with it. Emphasis has been made that the chief indication for cholecystectomy is calculous cholecystitis, but one also has to consider the symptomatic non-acute acalculous gallbladder, particularly those showing nonfunction with the dye test on at least two occasions. (If the history is fairly characteristic and all other possibilities ruled out, the dye test is positive and no other cause is found at operation, the gallbladder should be removed.) Cholecystectomy eliminates the possibility of future disorders such as acute cholecystitis or cholelithiasis, or doubt as to the cause of any postoperative symptoms. Any possible harm done will be less than the chance of clearing up the symptomatic condition. The causes of symptoms in the group under study are not well understood. How much infection is necessary to produce symptoms, what part stasis and varying biliary tensions play, what are the effects of minor and periodic obstruction of the cystic or common duct, and many other questions are still to be answered.

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DISCUSSION

Joel W. Baker (Seattle, Wash.): Dr. Madding has analyzed a problem that will occasionally confront every surgeon performing abdominal surgery.

There appears to be an irreducible minimum of from 3 to 6 per cent in all reported cholecystectomy series in which the gallbladder is grossly if not also microscopically normal. Several years ago Dr. Gibbons and I found eighteen (3 per cent) of 542 gallbladders removed at the Virginia Mason Hospital to be grossly normal, and thirteen of the eighteen were equivocal also on microscopic examination. As in Dr. Madding's series, some of these patients had not had the benefit of the Graham-Cole test. In addition to these eighteen stoneless, chronic cases, there were fourteen acutely inflamed gallbladders, two of which had frank empyema, and five with gangrene, all without stones, certainly attesting to the fact that function may be lost and disease ensue independently of the formation of stones. Gross stricture of the cystic duct was convincingly recorded in only one of these cases. It is interesting that ascariasis was present in the common duct of one patient.

I think it should be emphasized that in Dr. Madding's concluding recommendation for cholecystectomy he has clearly stated he refers to the gallbladder that is suspect on the basis of symptoms and has failed to function on at least two cholecystograms. I do not believe laparotomy should be performed in such cases solely on the basis of a poorly functioning gallbladder, but only after the repeated tests show *no* function. In the absence of other lesions to explain the patient's symptoms we would then concur on cholecystectomy and would emphasize a few points from our experience. (1) Doubling the dose of the Telepaque® when the test was repeated did not enhance its value in our experience. In 90 per cent of those patients with repeated tests showing non-function, the gallbladder was found to have stones at operation. Pathologic lesions of the gallbladder, including polyps, cholesterosis or cancer, were discovered in most of the remaining 10 per cent. (2) Repeatedly, we have been convinced that the surgeon, by palpation of the distended or partially distended gallbladder, cannot rule out small stones. In one case a stone was demonstrated by the Graham-Cole test yet neither I nor my two assistants could demonstrate this stone by careful and repeated palpation until the gallbladder had been aspirated. (3) In the series of our 500 cases just cited, there were two with normal acalculous gallbladders in which a stone was recovered from the common bile duct. In Dr. Madding's series there was one case in which a common duct stone was recovered a year later. For this reason I would like to ask him if he would consider and discuss a sixth alternative recommendation to the five he has reviewed, that is, to remove the gallbladder in these bizarre cases, as he concluded, but to make use of the cystic duct for an operative cholangiogram at the same time. This may be a controversial subject but I personally believe it has a definite place in this unusual situation. The cholangiogram plus the liver biopsy he has suggested, reinforced by a most careful exploration of the esophageal hiatus, the pancreas, stomach, duodenum and other abdominal viscera, as he has mentioned, should result in fewer patients suffering from unexplained persisting symptoms. It is in just such equivocal cases that the more complete picture afforded by operative

cholangiography becomes of obvious value in reducing unnecessary secondary operations on the biliary tract. Since the gallbladder is but part of the biliary system, it might seem that preoperative symptoms sufficient to justify the removal of a grossly normal gallbladder would also speak for this visual information about the rest of the tract. It would eliminate the question of unnecessary instrumental opening of the common duct in these borderline cases. It would provide a permanent record of the size and emptying of the intra- and extrahepatic ductal systems.

In summary, we would not operate for vague gastrointestinal symptoms without first having at least two reliable, positive Graham-Cole examinations. At operation we would not depend upon palpation of the fasting, distended gallbladder to rule out the presence of small stones. If no other explanation of symptoms is found within the abdomen, we would remove the gallbladder and also take an x-ray of the bile duct. Those who have served on Hospital Tissue Committees will agree that in the operative record should be carefully listed the reasons justifying the removal of a grossly normal organ.

I am indebted to Dr. Madding for bringing this problem into focus and offering a rational method of dealing with it. He has supported his recommendations by the opinions of a number of authorities.

KIRK H. PRINDLE (San Mateo, Calif.): It does not seem to me that one can argue with removing an innocent-looking gallbladder when no stones are found, especially after adjacent possibilities for the cause of the symptoms have been eliminated. However, I would like to make two points: first, fifteen surgeons found gross evidence of disease in 92 per cent of the thirty-five cases that Dr. Madding called macroscopically non-pathologic. This was in the nature of adhesions about the gallbladder, thickening and scarring. Eighty-three per cent of the thirty-five cases had microscopic evidence of inflammation. These figures do not seem to justify a category of macroscopically non-pathologic disease.

Second, the author, in his review of the records, states that all of the thirty-five cases classified as macroscopically non-pathologic had a history of gastrointestinal disease, yet more than half had no tenderness in the right upper quadrant and no history of biliary colic. Ten of the thirty-five patients had no cholecystograms; twenty-three of the thirty-five had some evidence of impaired filling.

There was no mention of repeat cholecystograms in these cases under discussion or other special studies such as double-dose dye, etc.

All of this suggests to me that the indications for surgery in this group were not always clear-cut, and I wonder if Dr. Madding would not agree.

CHARLES E. MACMAHON (Seattle, Wash.): I would like to call attention to the fact that all pain in the right upper quadrant is not of intra-abdominal origin, and cite as evidence two unfortunate cases of my own.

In one year at Swedish Hospital we had three patients with congenital absence of the gallbladder. (I treated two of them and Dr. John Duncan one.) They all had Graham-Cole tests which obviously showed a non-functioning gallbladder since it was absent.

In my two cases the cause of the pain in the right upper quadrant was the prodrome of right heart failure as was demonstrated in the immediate postoperative period to our great distress.

GORDON F. MADDING (closing): The 6.1 per cent of cases of cholecystectomy falling into the non-acute and acalculous group is too high. A more complete study of some patients in this group should have been made from a roengenographic standpoint. With present methods of study, approximately 2 to 4 per cent of all gallbladders removed will fall into the non-acute and acalculous category. Until our knowledge is greater concerning all causes of biliary tract dysfunction and discomfort, this should remain an acceptable figure.

Acute Cholecystitis in a Municipal Charity Hospital

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THE treatment of acute cholecystitis remains a frequent challenge. Despite almost general agreement as to the advisability of early surgical therapy, difficulties in diagnosis and in predicting the course occur often enough that continued re-evaluation of the disease seems warranted. We have reported on this problem previously [1,2]. Our policy has been early surgery for patients who have been ill for three days or less. We keep under observation those patients who have been ill for a longer time and operate only if there is definite evidence of progression of the disease. Since adopting this policy, we have treated an additional 123 patients on the surgical wards of the University of California Service at the San Francisco General Hospital. This is a charity hospital and urgent medical problems far exceed the elective. During recent years, the number of patients with acute cholecystitis has exceeded the number with the chronic condition. The present report is a review and comparison of findings and results.

DURATION OF ACUTE ATTACK

In some instances the time of onset is difficult to ascertain, especially in elderly patients with coexisting diseases, but most of the histories are reliable. Figure 1 shows the time elapsed from onset of the acute attack until entry into the hospital. Comparison of the two periods shows similarity in this respect. Of 217 patients only 41 per cent entered the hospital during the first twenty-four hours of the attack, and 74 per cent entered during the first seventy-two hours. This delay is frequently attributed to the patient's experience of a similar attack that subsided spontaneously. Several patients were transferred from hospitals for the chronically ill.

The figures within the white squares represent the number of deaths. As might be expected, the number of deaths increased as the duration of the acute episode increased.

AGE AND SEX OF PATIENTS

Cholecystitis is more frequent in women and in older people. (Table 1 and Fig. 2.) Fifty-eight per cent of the patients on our wards were sixty years old or more. (Table II.) Males comprised 24 per cent of our patients less than sixty years old and 43 per cent of those more than sixty years old. Figure 2 graphically presents the number of deaths in the various age groups.

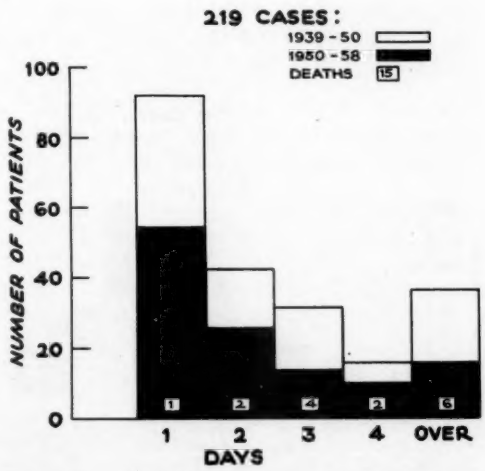

FIG. 1. Time elapsed between onset of acute attack and entry into hospital.

TABLE I
SEX OF 217 PATIENTS WITH ACUTE CHOLECYSTITIS (1939–1958)

Sex	1939–1949 (No. of Cases)	1950–1958 (No. of Cases)	Combined	Per cent
Male.....	32	45	77	35
Female....	62	78	140	65

TABLE II
AGE AND SEX OF 217 PATIENTS WITH ACUTE CHOLECYSTITIS (1939–1958)

Age (yr.)	Total (No. of Cases)	Per cent	Female (No. of Cases)	Male (No. of Cases)	Per cent Male
Less than 60.....	90	42	68	22	24
More than 60....	127	58	72	55	43

TABLE III
INCIDENCE OF LITHIASIS FOUND AT OPERATION (108 PATIENTS)

Findings at Operation	No. of Patients	Per cent
Stones in gallbladder.....	102	94.4
Stones in common duct (silent)...	8	7.4
Acalculous.....	6	5.8

DIAGNOSIS

The diagnosis is usually quite evident. A rounded tender mass was palpable in 40 per cent of the last 123 patients; often rigidity was so pronounced that a mass was obscured which did not become palpable until relief of pain. Absence of a tender mass quite often makes the differential diagnosis more difficult. If the mass is still present when symptoms subside, it may indicate that the pathologic process is increasing.

Intravenous cholecystography was helpful in a few cases in which the diagnosis was in doubt. Intravenous cholangiography was used in sixteen patients, mainly those suspected of harboring a silent common duct stone. Clinical evidence of jaundice was not present in any of these patients. The gallbladder was not visualized in any of the patients but the common duct was adequately demonstrated in seven.

COURSE OF THE DISEASE

The severity and course of the acute attack may be influenced by the severity of the chronic gallbladder disease present at onset.

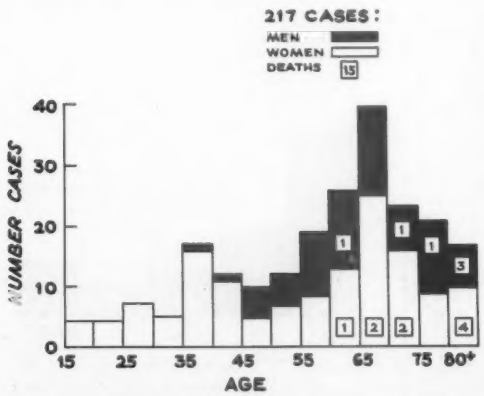

FIG. 2. Number of deaths in various age groups.

In the young patient with biliary tract disease, stones may be present in a gallbladder whose wall may show only mild reaction. On the other hand, in patients with long-standing biliary tract disease and repeated attacks, the wall of the gallbladder becomes scarred and less elastic. Acute obstruction is less well tolerated in these patients because of the nature of the existing pathologic process in the biliary tract and because the inflammation may be more severe. A history of long-standing biliary tract disease was elicited from 79 per cent of the patients. The impact of acute cholecystitis is greater in older patients since usually they have had biliary tract disease for several years.

Obstruction of the cystic duct by stone was the precipitating factor for the majority of patients operated upon for acute cholecystitis. (Table III.)

In six patients no stones were found at the time of operation, although the tenseness of the gallbladder suggested obstruction of the cystic duct. Acalculous acute cholecystitis seemed clinically indistinguishable from calculous acute cholecystitis and the pathologic alterations were similar. Results of culture studies of bile obtained from the gallbladder at the time of operation are shown in Table IV.

TREATMENT

Several factors have influenced us in the selection of therapy for any given patient.

TABLE IV
BACTERIAL CULTURES OF BILE (68 PATIENTS)

Results of Cultures	No. of Cases	Per cent
Positive	45	66
No growth	23	34

TABLE V
OPERATIVE PROCEDURES (101 PATIENTS)

Operative Procedure	No. of Patients	Per cent
Cholecystectomy	61	60
Cholecystostomy*	40	40

* Cholecystectomy later in sixteen patients.

Ideally, one would prefer to operate at a time when the acute inflammatory reaction of the gallbladder is minimal and any other coexisting diseases have been evaluated and treated. A few patients have symptoms and signs of acute obstruction that are minimal or of decreasing severity when they are first examined. Observation for a few hours may indicate that the acute obstruction is relieved. The patient may then be treated conservatively. We have advised such patients to have an elective operation after complete recovery from the acute episode. Spontaneous relief of the obstruction is more likely in younger patients.

We regarded operative intervention as imperative for patients who gave a history of long-standing biliary disease or previous acute episodes. In patients with such histories, there were severe pathologic changes in the gallbladder before the onset of acute obstruction. Spontaneous relief of the obstruction was less likely in these patients and the danger of early gangrene and perforation were increased.

The patient's general health before the onset of the acute episode has also influenced our choice and timing of treatment. In this hospital, we have found a high incidence of cardiac disease, hypertension and obesity especially in elderly patients. The prolonged discomfort of acute cholecystitis may have an adverse effect on patients with cardiac disease or reduced vital capacity. We believe that early relief of pain by operation has been beneficial for many elderly patients or for patients who ordinarily would not be considered good candidates for operative treatment.

The acute episode subsided in twenty-one patients and early operation was not necessary. Six of these patients had elective cholecystectomy performed later. The remaining patients were judged to have continuing inflammation. After evaluation, relief of pain and preparation, operative treatment was instituted. Most of these patients (75 per cent) were operated upon within twenty-four hours of entry.

The choice of operative procedure (Table v) has been cholecystectomy and, when indicated, exploration of the common duct.

Cholecystostomy was employed in forty severely ill, elderly patients for whom we believed general anesthesia or a long operation would be detrimental. Cholecystostomy was also used in some instances in which we encountered perforation of the gallbladder or intense inflammatory reaction over the region of the common duct, and in a few elderly patients suspected of harboring common duct stones. Drainage of the gallbladder allowed decompression of the biliary passages and subsidence of the acute episode. Adequate cholangiograms were then possible during convalescence.

Clinical jaundice was noted infrequently in the patients with acute cholecystitis. We explored the common duct in four patients at the time of operation for the acute episode and found stones in two. Exploration revealed stones in six of eight additional patients after the acute episode had subsided.

In patients whose acute attack subsided during observation or after cholecystostomy, our experience paralleled that of Ross, Boggs and Dunphy [3], who demonstrated that the chronic pathologic process in the gallbladder persisted despite subsidence of an acute episode; we therefore advised cholecystectomy within a reasonable time.

We have been impressed by the rapidity of change in the clinical course in certain cases, best illustrated by several elderly patients who were under observation and in whom the acute attack appeared to be subsiding. In these patients the temperature rose rather abruptly, the pulse became rapid and they appeared lethargic. Often we suspected that the acutely inflammed gallbladder had perforated, but usually no perforation was found. These changes may have been due to cholangitis and probably represented a minor component of the shock-like episode that occurs in the course of

TABLE VI.
ANALYSIS OF MORTALITY IN 123 PATIENTS WITH ACUTE CHOLECYSTITIS (1950–1958)*

Sex, Age (yr.) and Onset of Illness	Preoperative Data	Operation	Cause of Death
F., 82, ill 9 days before entry	Cardiac decompensation, digitalis 2 days, temperature 103°F.	Cholecystostomy	Septicemia, abscess, thrombophlebitis, pneumonia
F., 88, ill several days before entry	Cardiac disease, nephritis, senile dementia, diagnostic problem, suddenly patient became very ill	Cholecystectomy	Pneumonia, nephritis
F., 66, ill 3 wks. before entry	Senile dementia, anemia, symptoms thought to be subsiding then patient became very ill	Cholecystostomy	Pneumonia, uremia
F., 87, ill 4 days before entry	In convalescent home, auricular fibrillation became more acute	Cholecystostomy	Cerebrovascular thrombosis, pneumonia
F., 68, ill several days before entry	Disoriented, senile, persistent vomiting	Cholecystostomy	Cerebrovascular thrombosis, pneumonia
M., 76, ill 8 days before entry	Hypertension, hemiparesis, symptoms subsiding (questionable), sudden temperature of 103°F.	Cholecystostomy	Peritonitis, gastrointestinal hemorrhage

* Six deaths, 4.8 per cent.

severe cholangitis due to a common duct stone and infection. In ten of our more recent patients we have obtained a biopsy specimen of the liver at the time of operation. Common duct stones were not present in any of these patients. Microscopic sections of the liver demonstrated a periductal inflammatory reaction in six patients. Inflammatory changes in the periductal tissues of the liver corresponded to the stage of inflammation in the wall of the gallbladder. In three patients we found extensive polymorphonuclear infiltration of the wall of the gallbladder, periductal tissues of the liver and deposits of similar cells in the hepatic ducts. In an additional three patients a similar chronic inflammatory reaction was found.

We believe that antibiotic therapy is indicated in an attempt to prevent or control septic complications. In a previous report, Goldman et al. [4] reviewed the results of the bacteriologic studies at this hospital. Positive cultures were more frequent from the fourth to the eight day of the disease and least common during the first three. Studies of gallbladder bile for antibiotics revealed a significant concentration in only a few instances; antibiotics were found often enough in sufficient numbers, however, to warrant their continued use.

DEATHS

We have previously reported a study of 225 patients with acute cholecystitis who entered the hospital from 1936 to 1950, with a mortality of 9.3 per cent from 1936 to 1946. With a change to our present method of treatment the mortality was 3.1 per cent from 1946 to 1950. In the past eight years, 1950 to 1958, six deaths occurred among 123 patients (mortality 4.8 per cent, Table VI). All the patients who died were sixty-five years old or more. Three were more than eighty years old. Two had been patients at hospitals for the chronically ill and one was confined to bed or wheel chair by paresis. Glenn and Wantz [5], who reported a mortality of 1.4 per cent in patients less than fifty years old and 4.9 per cent in patients more than fifty, stated that about half these deaths could be attributed directly or indirectly to perforation. Strohl and Diffenbaugh [6], Dunphy and Ross [7], and Boyden [8] in reports of experiences with acute cholecystitis likewise cite perforation as a major factor in the fatal cases. Several factors tend to make perforation more likely in many older patients, chief of which is the advanced chronic cholecystitis present at the time of onset of the acute obstruction.

A second factor, perhaps just as important as a cause of death, is the effect of the pain and incapacity caused by the acute episode. Splinting of the diaphragm, lowered vital capacity, and possibly decreased cardiac efficiency aggravate pre-existing disease or encourage thrombosis and embolism.

Previous or long-standing biliary disease in

many of the older patients may have resulted in hepatic damage and a more severe reaction to an acute episode.

All patients in this group who died had one or more unrelated illnesses. In some of these patients the operative procedure was deemed necessary to prevent what appeared to be a certain fatal outcome. Cholecystostomy to establish drainage was performed in five patients and cholecystectomy was performed in the remaining patient.

Only two of the deaths appeared to be a direct result of perforation. The other deaths could easily be attributed to coexisting illnesses that were adversely affected by the acute inflammatory reaction. All the patients who died had been ill for several days.

SUMMARY

The clinical course of 123 patients with acute cholecystitis is reviewed. Fifty-eight per cent of the patients were more than sixty years of age and 65 per cent of the fatalities occurred in women. With increasing age there was a relative increase in the percentage of male patients.

The diagnosis was usually quite clear. A mass was palpable in 40 per cent of the patients. Subsiding symptoms with persistence of the mass were thought to be indicative of progressing inflammation.

Intravenous cholangiography was helpful in the diagnosis. Of sixteen patients with acute cholecystitis, the common duct was clearly demonstrated in seven.

Common duct stones were found in 8.7 per cent of the patients.

Progression of the inflammation of acute cholecystitis was more severe and rapid in elderly patients. This was thought to be due to the more advanced state of the chronic pathologic process in the gallbladder in the older patients which was caused by long-standing biliary tract disease.

A sudden change in the clinical course of certain older patients was attributable to cholangitis. At operation for acute cholecystitis, a biopsy specimen of the liver was taken in ten recent patients. Microscopic evidence of cholangitis was found in six patients.

Cholecystectomy was possible in 60 per cent of the patients and exploration of the common duct was carried out in four, at the time of operation. Cholecystostomy was the operation of choice in the remainder of the patients.

Among 123 patients with acute cholecystitis there were six deaths (mortality 4.8 per cent). All the patients who died were more than sixty-five years of age and had been ill for several days before entry. The deaths were related to peritonitis or aggravation of pre-existing unrelated diseases.

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DISCUSSION

Henry H. Searls (San Francisco, Calif.): When the consultant is confronted with a patient who has an acute inflammatory condition in the right upper quadrant of the abdomen, he must arrive at a positive diagnosis. He will have to consider duodenal ulcer, acute pancreatitis, acute pyelitis and coronary occlusion. Space does not permit a discussion of the differential diagnosis but I would like to point out, as has Ochsner, the extreme danger of confusing acute coronary disease with acute cholecystitis, with obviously disastrous results.

The experience of the authors has been extensive and as they have gained it they have become more inclined toward surgical treatment. However, one can find many articles in which a much greater conservatism is recommended. Notably, Lee* reported on 691 cases in which cholecystostomy was the only surgical treatment performed and then only for fulminating disease in old patients. I have always believed that experience in a county type of general hospital in which patients are older and usually in poorer health leads the surgical staff toward more radical treatment. In managing a fairly large series of private patients I have not experienced this urgency and have been content to delay operation unless progression of symptoms and findings demands action. In operating for acute cholecystitis, surgical demonstration of the ductal

* Lee, A. E. The management of acute cholecystitis. *Brit. J. Surg.*, 45: 523–527, 1958.

system, portal vein and cystic artery may be made far more difficult by the presence of retroperitoneal edema and other products of acute inflammation.

Such a reaction usually persists for several months and the slow resolution of inflammation extends far past the complete subsidence of the clinical symptoms. Surgical treatment should include continuous gastric suction, sedation by Demerol® and barbiturates, and extensive use of antibiotics. After removal of the gastric tube the diet should be fat-free. Subsequent cholecystographies should not include the usual technic of the fatty meal to demonstrate emptying of the gallbladder.

In reviewing the literature it is noted that all authors emphasize the increased hazard associated with acute cholecystitis in elderly patients. In such patients, therefore, adoption of conservative therapy must be associated with extreme caution and almost continuous observation of the patient.

MARTIN A. HOWARD (Portland, Ore.): When I noted the work being done by my good friends, Drs. Goldman and Lyon, I became interested in what occurs in a general hospital such as Good Samaritan Hospital in which there are a good many surgeons, and one does not have the control that one has in a university hospital. I looked up our cases during the last ten-year period, and there were 247 patients with acute cholecystitis admitted to Good Samaritan Hospital.

I divided these patients into three different groups. The first underwent immediate surgery, including cholecystectomy (forty-nine cases) and cholecystostomy (nineteen cases). One might almost state that these patients underwent emergency surgery.

Delayed surgery was carried out in 179 cases of which there were two different groups because the delay extended from about five to perhaps ten days. Some of the delay occurred in my own patients. We had fifty-seven patients in what one might call the intermediate group, and there was a conservative group of 122 patients.

I was pleased that Dr. Searls believes there is a good place for conservative treatment. In studying some of these patients it was my belief that many had had their acute attack for several days which accounts for the more conservative approach.

If a relatively mild acute attack is indicated, chances are good that it has only been going on a few hours, in which case early cholecystectomy should certainly be carried out. If the patient is very ill, temperature is high and one believes that the attack has been continuing for several days, the patient should probably be observed for at least twenty-four to forty-eight hours. If the temperature falls, and the white blood count and the sedimentation rate continue to fall, perhaps conservative treatment could be carried out and surgery performed at a later time. There are several reasons for this: First, all of us who have operated upon patients with acute attacks have found that we have had to drain the gallbladder and continue the procedure later. Two operations are necessary in some cases. Second, if you have a concurrent common duct stone it may be well to let the attack subside. Then in about six to eight weeks surgery may be carried out with safety. In conclusion it seems to me that exploration of the common duct may be performed much more easily and safely at that time.

As Dr. Coller stated several years ago, when he called attention to the fact that many common ducts were injured during operative removal of the acutely disturbed gallbladder, it probably would have been much better if the gallbladder had been drained.

OTTO H. PFLUEGER (San Francisco, Calif.): I would like to discuss an extremely interesting and rare problem that we have seen within the last few months. As a matter of fact the pathologist who performed the autopsy on this patient stated that after a perusal of the literature that she had not found a similar case presented.

The patient was a sixty-eight year old woman who came into the hospital one evening with a twenty-four hour history of pain in the right upper quadrant with nausea and vomiting. She had mild icterus and a palpable mass in the right upper quadrant. Temperature, pulse, respiration and white blood count were normal. However, she did have a high polymorphonuclear leukocyte count.

The following morning she felt perfectly well and the mass was gone. One could not feel it at all, and she appeared to improve for four days, after which the whole episode recurred in the very same way with a large mass palpable in the right upper quadrant. Jaundice reappeared and her condition very, very rapidly worsened; as a matter of fact she became so sick so very quickly that the medical personnel believed she presumably had hepatic disease, perhaps something like acute yellow atrophy, rather than biliary tract disease *per se*.

At postmortem examination, a bulge was noticeable in the duodenum obviously indicating that something was attempting to get out of the common duct.

There was a tremendous blood clot in the common duct which produced complete obstruction of the common duct with marked dilatation behind it. There was a further clot in the common duct at the junction with the cystic duct.

The gallbladder, itself, contained dark brown bile. There were no stones present. This hemorrhage and obstruction were due to a Clostridium welchii infection.

ALLEN M. BOYDEN (Portland, Ore.): I have been fortunate enough to have had charge of the biliary

trait service in surgery at the Multnomah County Hospital for some eight years, and for that reason perhaps have the privilege of making one small comment in relation to this paper.

Whether one agrees with their immediate or relatively immediate approach to the acute condition of the gallbladder or whether one follows the more conservative suggestion of Dr. Searls and a number of others in the literature, there is one point that I think that we have learned which has been of tremendous advantage in the aged patient, particularly those with other diseases such as diabetes, nephritis, uremia, heart disease and so forth. When one decides to operate on such a patient, whether because conservative treatment has failed or because one believes they should all be operated upon early, one can save lives by performing what we like to call "elective cholecystostomy" instead of the backing-out procedure that is so commonly performed.

It is my belief that much of the hazard to these old patients is related to the incision one makes and not to what else is carried out. In other words, a long right upper rectus incision in such an infirm patient may produce serious complications whether one drains the gallbladder, or removes it, or whether one drains the common duct. We like to approach this problem by making a small incision over the gallbladder mass with the definite purpose of performing cholecystostomy, often under local infiltration and intercostal block. One can always advance from here, but one never has to back out of a deep situation when the risk proves too great.

I hope before too long to be able to present our data illustrating improved results by following this procedure in many of these poor risk patients.

Donald T. Hall (Seattle, Wash.): I should like to make one or two very brief comments on subjects about which I feel rather strongly.

I think we would do well to be a little more forceful in our approach to our medical colleagues and emphasize to them the relationship of age to morbidity and mortality in this disease.

In the last six months I have operated upon three women with jaundice and acute cholecystitis, one of whom was eighty-four, one eighty-five and the third ninety years of age. Subjecting people of this age to such an operation seems needless if prophylactic cholecystectomy had been performed when they were having symptoms at a considerably younger age. However, many of our medical colleagues are prone to watch these people through one attack after another and even suggest that they should not be operated upon because they have reached seventy or more years of age.

Insofar as I personally am concerned I do not think chronological age has as much to do with the risk as some other things. I would much prefer to operate on a slender, wiry eighty year old patient than I would on an obese person in his sixties. Fortunately, most patients in this age category including the three previously mentioned are of this habitus.

As Dr. Boyden has mentioned, I strongly believe it is the incision in the abdominal wall that injures these people insofar as the operative procedure is concerned. I have always felt strongly about the advantages of transverse incisions and postoperatively they certainly are better. At least my patients were out of bed within the first two or three days, and all fortunately had a successful outcome.

I am certain that if we do not keep these facts of morbidity and mortality before our medical colleagues, we are going to be forced to operate on these people when they do reach the age at which morbidity and mortality are unnecessarily high.

Leon Goldman (closing): We agree very heartily with Dr. Boyden and in most of these cases cholecystectomy was performed in exactly the manner that he described. The operation was performed electively through a short subcostal incision with the patient under local anesthesia.

However, there are other patients for whom technically it would be rather hazardous to attempt cholecystectomy even though their general condition is quite good. Despite the fact that the incision is ample enough to permit the performance of cholecystectomy we believe it is wiser to carry out the lesser procedure.

What we have said about acute cholecystitis in a county or city hospital of course applies elsewhere. In dealing with younger patients I think that we can even take a more active surgical viewpoint than that mentioned by Dr. Searls. However, even in young patients who are in good condition but who have had the disease for a few days, we now believe that one should not hesitate to operate and usually one should perform cholecystectomy. It takes a long time for this process to be resolved. The patient should have a long period of hospitalization followed by another period of hospitalization. The incidence of subphrenic abscess, intraperitoneal complications or perforation of the gallbladder is now much lower than was reported previously. Of course all of us are aware that we must be careful to identify the vital structures during this procedure.

In comparison with younger patients, however, we make an exception in elderly patients whose symptoms are subsiding. In the latter case, we allow the symptoms to subside completely and then we perform the complete operation that Dr. Howard mentioned. In younger patients we do not believe it necessary to postpone surgical treatment of the same type of process. The only deaths in this series occurred in patients more than sixty years of age, which accentuates some of the differences in the elderly group as compared to the younger group. I wish to thank the discussers for their remarks.

Effect of Pancreatic Secretions on the Gallbladder in the Absence of Bile

JOHN M. GOIN, M.D., JOHN Q. OWSLEY, M.D., JACKSON CRANE, M.D., JOHN S. NAJARIAN, M.D. AND H. J. MCCORKLE, M.D., *San Francisco, California*

From the Surgical Research Laboratories and the Department of Surgery of the University of California School of Medicine, San Francisco, California. Supported by the Christine Breon Fund for Medical Research.

A NUMBER of investigators [4–6] have described the effect of instillation of pancreatic and duodenal juice into the gallbladder of experimental animals. Some of these experiments resulted in the production of cholecystits and others did not. Colp and Doubilet [1,8], and others have discussed the clinical importance of biliary pancreatic reflux in the production of acute cholecystitis.

In 1940, Bisgard and Baker [1] described the effects of ligation of the common bile duct in young goats. (Fig. 1A.) Because of the peculiar anatomic arrangement of the goat's biliary tract (Fig. 2), this experimental procedure resulted in the mixing of bile and pancreatic juice in both the biliary and pancreatic duct systems, and pancreatitis and cholecystitis occurred. These authors concluded that neither stasis of bile nor the reflux of pancreatic juice into the biliary system alone produced cholecystitis, but when both were present cholecystitis always resulted.

Whitrock et al. [3] observed the development of cholecystitis as an incidental finding while studying the effect of bile flowing through the pancreas of the goat. In their experimental preparations reflux of pancreatic juice into the gallbladder probably occurred. (Fig. 1B.)

More recently, Najarian et al. [2] ligated the distal part of the common duct in young goats and drained the goat's gallbladder with a Roux-Y cholecystojejunostomy, thus allowing the gallbladder to be exposed to a mixture of bile and pancreatic juice without stasis. (Fig. 1C.) Cholecystitis developed in all of their animals.

The following experiment is a continuation of the previously reported studies of Najarian and Whitrock on the effect of the flow of pancreatic secretions through the gallbladder of living animals. Najarian found that the flow of mixed bile and pancreatic juice through the goat's gallbladder produced cholecystitis. In the following experiment only pancreatic juice was permitted to flow through the gallbladder; bile was excluded.

Kid goats three to four months old were used as experimental animals because disease of the gallbladder does not occur in them, and the anatomic arrangement of the goat's biliary duct system is particularly adapted to a study of this kind. (Cholecystitis may occur spontaneously in older goats.)

The animals were anesthetized* with intravenously administered sodium pentobarbital. The experimental surgical procedure consisted of ligation of the common bile duct at its distal end, transection of the common hepatic duct with ligation of its distal end, and Roux-Y anastomosis of its proximal end to jejunum; a Roux-Y cholecystojejunostomy also was performed. (Fig. 3.) This prepartion allowed only pancreatic juice to pass through the gallbladder. The bile was diverted away from the gallbladder directly into the intestine. Control subjects were normal goats in which only cholecystojejunostomies were performed.

* Tracheostomies were performed to prevent the accumulation of tracheobronchial secretions during anesthesia. After five consecutive deaths in the immediate postoperative period it was apparent that these animals had fatal pulmonary complications due to partial or complete occlusion of the rubber tracheostomy tubes with mucus. Consequently the remaining goats were operated upon without tracheostomy with the result that there were no more postoperative deaths attributable to pulmonary causes.

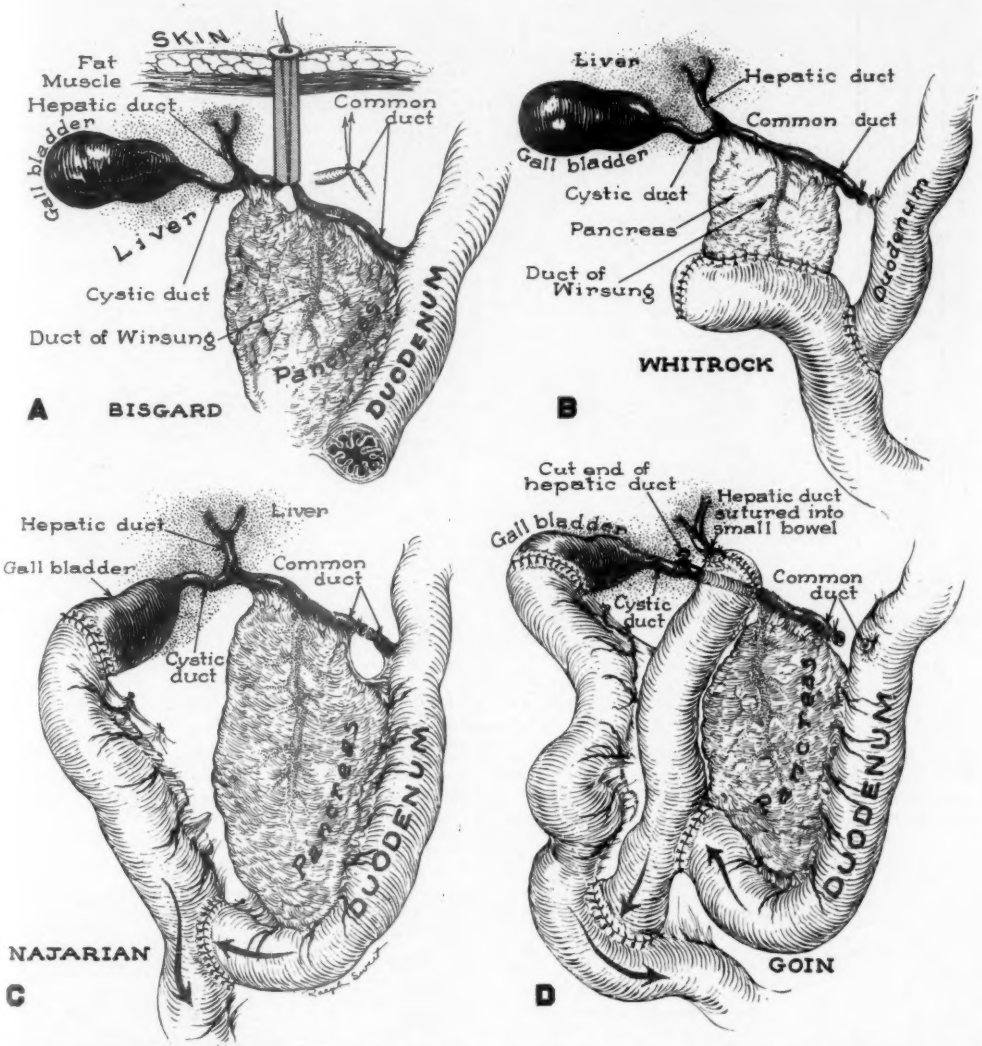

FIG. 1. A comparison of the surgical methods for producing experimental cholecystitis or pancreatitis in young goats. A, Bisgard and Baker. B, Whitrock et al. C, Najarian et al. D, Goin, Owsley, Crane, Najarian and McCorkle.

The animals were sacrificed at periods varying from two to seven weeks after the surgical procedure. Serum amylase and bilirubin values were determined at weekly intervals, and bacteriologic and pathologic studies were made at necropsy.

With two exceptions* serum amylase determinations remained relatively constant during

*Goat No. 8 died two weeks postoperatively of diffuse peritonitis. Autopsy revealed a complete disruption of the anastomosis between the common hepatic duct stump and its segment of jejunum. There also appeared to be at least the junction of partial obstruction of the common bile duct by adhesive bands in the region of the common and cystic ducts. This probably accounted for the increased blood serum amylase. Goat No. 6 was sacrificed five weeks postoperatively. Clinically this animal appeared to be in good health and autopsy failed to show any cause for the serum amylase of 562 Somogyi units. Careful dissection of the common duct, cystic duct, gallbladder and cholecystojejunostomy revealed no sign of obstruction.

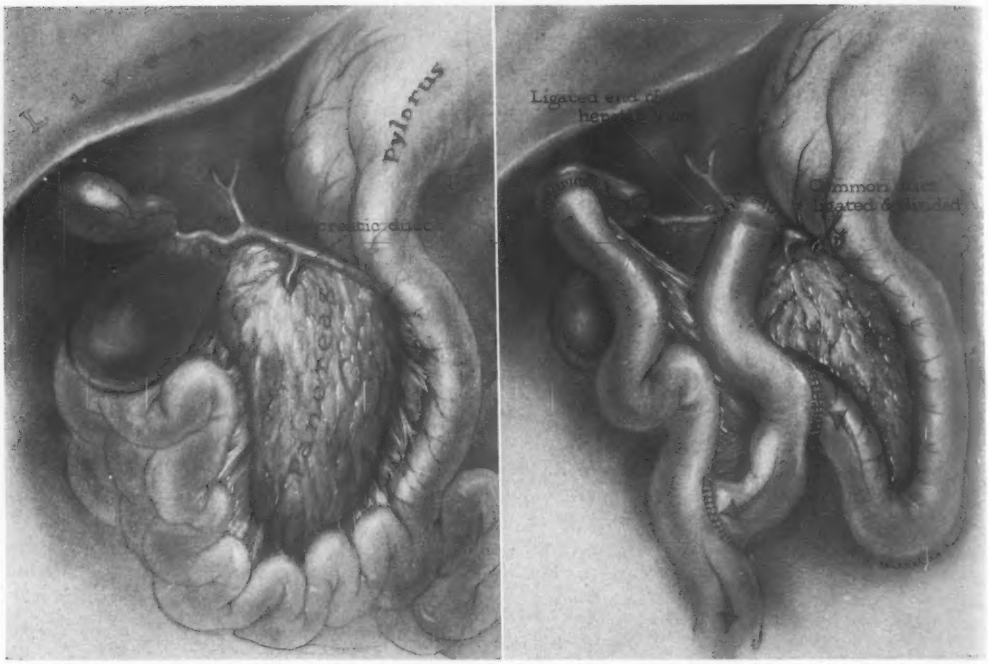

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FIG. 2. Diagram indicating anatomical relationships of the pancreatic and biliary ducts of normal goats. The common channel is significantly longer in the goat than in other experimental animals.

FIG. 3. Illustration of completed experimental procedure allowing pancreatic juice to flow through the gallbladder in the absence of bile. The distal end of the common duct has been ligated. The hepatic duct has been divided, its distal end ligated, and a Roux-Y anastomosis of its proximal end to jejunum performed. A Roux-Y cholecystojejunostomy and two enteroenterostomies restoring intestinal continuity complete the preparation.

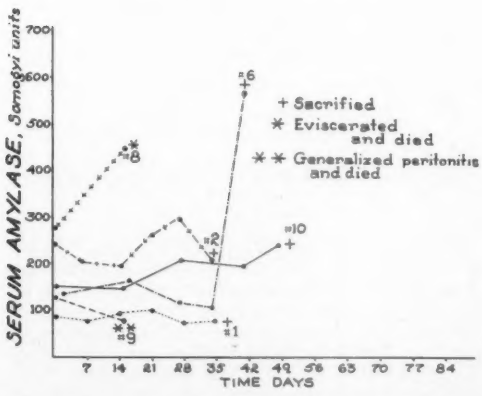

FIG. 4. Graph showing the results of serum amylase determinations made on kid goats in which surgical procedures were performed to allow pancreatic juice to flow through the gallbladder in the absence of bile.

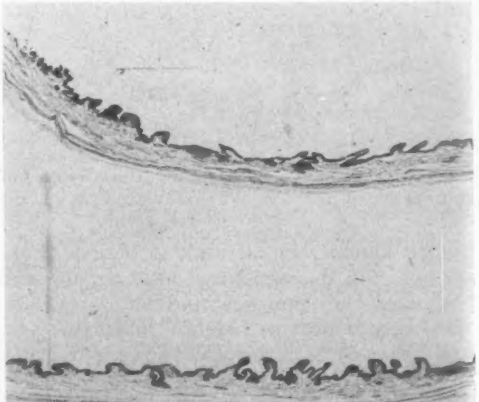

FIG. 5. Photomicrograph of the gallbladder in a normal goat.

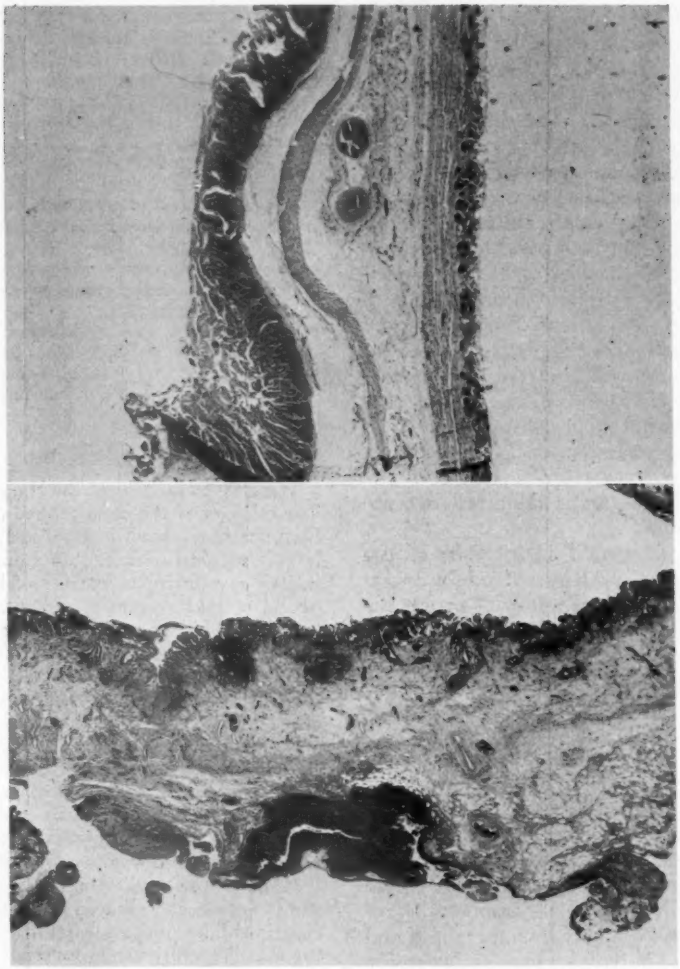

FIG. 6. Photomicrograph of the gallbladder in a goat in which a control cholecystojejunostomy only has been performed as a control for the experiment. The outer surfaces of jejunum and gallbladder are folded together. The jejunum with its promiment mucosa and muscularis appears to the left. The gallbladder is to the right. There is no evidence of inflammation.

FIG. 7. Photomicrograph of gallbladder of a kid goat in which pancreatic juice was made to flow through the gallbladder from which bile was excluded. There is villiform hyperplasia of the mucosa and definite focal aggregates of lymphocytes appear in the lamina propria.

the experiments. (Fig. 4.) The blood serum bilirubin values were normal in all animals.

The animals were sacrificed under anesthesia and aseptic conditions. Fluid was taken from the gallbladder and upper jejunum for bacterial cultures. In all animals cultures from both sites grew the same organisms, i.e., clostridia, enterococci and coliform bacilli.

The normal gallbladder of the goat is bluish and has very thin, translucent walls. The mucosa is pink with fine trabeculations. On microscopic examination (Fig. 5), the mucosa is

arranged in delicate villous folds and lines by a single layer of tall columnar cells. Occasionally the epithelium dips down into the deeper lamina propria to connect with small aggregates of simple mucous glands. The submucosa and muscularis are very delicate.

Roux-Y cholecystojejunostomy alone did not produce acute inflammatory changes in the gallbladder. Three months after Roux-Y cholecystojejunostomy had been performed the gallbladder walls were somewhat thickened and the mucosa was a deeper pink, with some degree of coarsening of trabeculations. Microscopically (Fig. 6), the gallbladder showed a somewhat more intricate mucosal pattern, with more numerous villous folds and epithelial lining cells that were somewhat hyperplastic. There was no evidence of inflammation of the lamina propria or the deeper mural structures. The submucosa and muscularis remained delicate as in normal animals.

Cholecystitis developed in all four of the experimental animals which survived the operative procedure to produce a flow of pancreatic juice through the gallbladder in the absence of bile. (The degree of inflammation observed in these gallbladders was not as severe as that produced by Najarian et al. [2] in their experiment in which bile mixed with pancreatic juice was allowed to flow through the gallbladder of kid goats.) No gallstones were found. The color of the gallbladders of these animals was bluish gray. There was considerable thickening and some opacification of the gallbladder walls. The mucosa was red and the trabeculae coarse and flattened. Microscopic examination revealed (Fig. 7) villous mucosal hyperplasia and focal aggregations of lymphocytes in the lamina propria. Fibrosis of the submucosa and muscularis was evident. Muscular hypertrophy was also present.

SUMMARY

An experimental method is described whereby bile was excluded from the gallbladder and pancreatic juice allowed to flow through the gallbladder of kid goats. Cholecystitis was produced but no gallstones were found.

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DISCUSSION

William P. Longmire, Jr. (Los Angeles, Calif.): The etiology of cholecystitis and cholelithiasis has been one of the most baffling and intriguing problems in medical science. It is a problem which has incited a voluminous amount of literature over a period of many years. The contributions of Dr. Goin and his associates to the elucidation of this problem give additional information which may help in explaining one of the most common pathological conditions encountered in the practice of surgery.

In the majority of cases, cholecystitis is associated with cholelithiasis and one would suppose there is a common etiological factor or factors. Whether cholecystitis without stones is based on a different pathological process or not, has been suggested but also awaits confirmation.

Many of the studies in which inflammation or stones have been produced in the biliary system of experimental animals seem to be so unrelated to the actual conditions encountered in man, that it is most difficult to assess their importance. Wangensteen and co-workers, from their observations in experimental animals and in man, have recently stressed the importance of narrowing and stenosis at the ampulla of Vater, with consequent stasis of bile, as an important factor in the etiology of biliary calculi. However, they do not imply any significance to reflux of pancreatic juice. They infer that stasis is the important factor.

Glenn summarizes the confused state of our knowledge on the subject quite well by stating, "No single theory provides an adequate explanation for all gallstone formations. Perhaps the most satisfactory explanation is that stone formation is the result of general variations from the normal functioning of the liver and biliary system. These may be the result of disturbances in metabolism, of infection, or of stasis or obstruction." Such a

variety of causes or combination of causes may well explain why it has been impossible to devise an experimental study that adequately reproduces, in the experimental animal, the situation encountered in man. The changes noted in the gallbladder under the experimental conditions here reported, are of interest particularly in the light of Bisgard's demonstration of cholelithiasis occurring in three of five goats in which the reflux of pancreatic juice into the gallbladder was produced.

The results presented would indicate to me that although active pancreatic juice flowing through the gallbladder can produce some degree of cholecystitis, it is unlikely that the presence of pancreatic juice in the gallbladder is an important factor in the production of cholecystitis or cholelithiasis in the usual patient with this disease.

JOHN S. NAJARIAN (closing): We agree with Dr. Longmire that the etiology and pathogenesis of cholecystitis is complicated, and concede that our present presentation is concerned with only one small part of a mechanism that may sometimes occur in some phase of the development of cholecystitis.

The Cystic Duct Remnant

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FOLLOWING removal of the gallbladder for cholecystitis and cholelithiasis, a small group of patients continue to have recurring bouts of distress in the right upper quadrant of the abdomen, indigestion and other symptoms usually ascribed to chronic disease of the gallbladder. When this sequence of events occurs, four possible explanations may be given. These are as follows: (1) residual common duct stone, (2) damage to the common duct, (3) error in initial diagnosis, and (4) presence of a large stump of cystic duct. The present report consists in a discussion of five cases where the symptoms of the patients were associated with a long remnant of cystic duct.

The exact frequency of this complication is difficult to estimate. Larmi and Fock [1] who reviewed this subject in 1958 found 241 cases in the literature and added thirteen of their own, a very small number considering the frequency of cholecystectomy. On the other hand as Glenn [2] has pointed out, while these case studies are made from University Surgical Services, by far the greatest number of cholecystectomies are performed at outlying hospitals and the late results are not known. What is apparently true in the New York area is equally true in San Francisco. One private hospital in this city reported 660 cholecystectomies during the five-year period 1953 to 1957, whereas the combined services of the University of California and Stanford University at the San Francisco General Hospital, having four times the bed capacity, reported only 241 cases. There are ten private hospitals in San Francisco.

The most common symptom in cases of cystic duct remnant is pain. The pain may be colicky, located in the right upper quadrant, and have the usual radiation to the back and to the scapular region. The pain does not usually appear immediately after operation, although this may be the case, but when it does occur, it is similar to the pain which the patient suffered before operation. The second most common symptom, according to the literature, is jaundice. While some workers such as Garlock and Hurwitt [3] have noted common duct stones in twenty-two of their thirty patients, none were noted by Morton [4] in his series or by Larmi et al. [1].

Because common duct stones are frequently present, there are those who do not believe that a cystic duct remnant alone will cause the symptoms described. Specht [5] and Millbourn [6] do not consider the evidence conclusive that a cystic duct stump will produce symptoms.

While not many surgeons have actually commented upon the length of the cystic duct stump that is left after cholecystectomy, among those who have Saegesser [7] simply stated "nicht zu nahe am choledochus." Judd [8] recommended ligation 2.0 cm. from the common duct, Maingot [10] at ⅛ inch, and Walters [9] at 0.2 cm. It has been our practice to ligate the cystic duct as closely as possible to the common duct without encroaching upon the common duct lumen.

Millbourn [6] examined 379 patients who underwent cholecystectomy by cholecystography and claimed that he demonstrated a cystic duct remnant in 78 per cent of the cases. The ducts averaged 2.7 cm. with a range of 1 to 11 cm. Calculi were found in only one patient.

In those cases in which the cystic duct remnant contains stones, it is easy to imagine that these stones are discharged into the common duct and that it is the presence of the stone in the common duct which is the cause of the symptoms. Where no stones are present, Womack and Crider [11] have suggested that there are actually small neuromas which are formed from the rich sympathetic plexus about the cystic duct, and that it is the irritation of

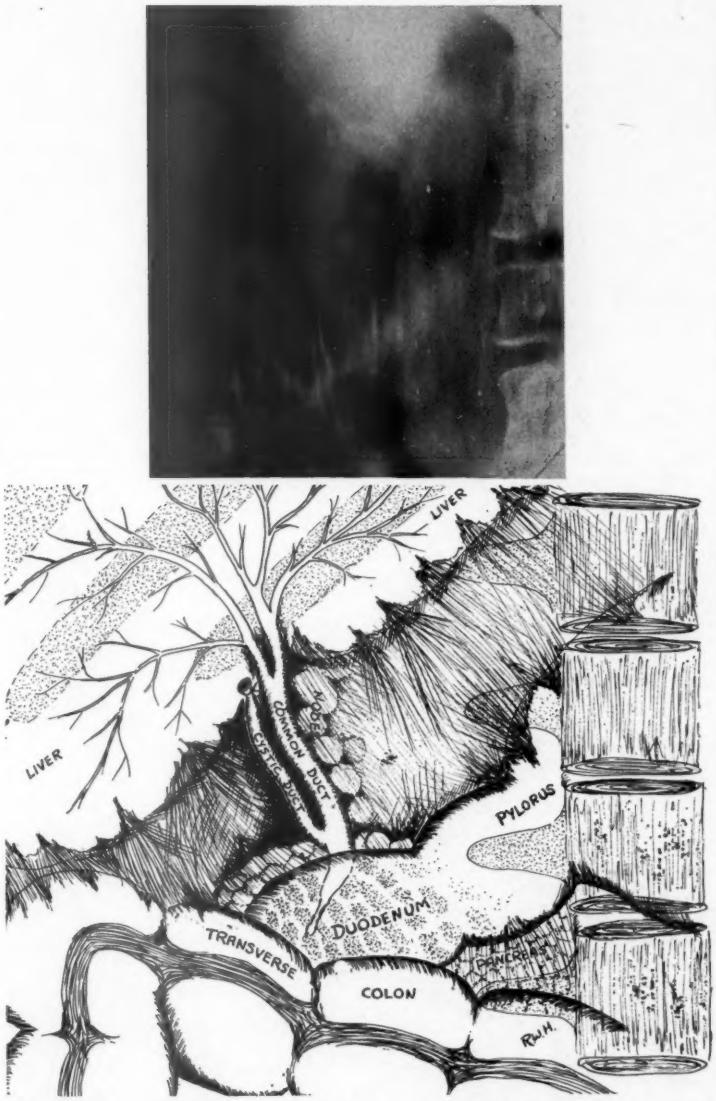

FIG. 1. Laminagram of intravenous cholangiogram and sketch showing long cystic stump in parallel to common duct.

these nerve endings that is responsible for the symptom complex.

CASE REPORTS

CASE 1. I. D. (No. 29117), a sixty-two year old white woman, entered Stanford University Hospital on May 17, 1958, with the complaint of intermittent pain of two years' duration in the right upper quadrant, radiating to the right scapular area. Seven years previously she underwent a cholecystectomy because of intermittent pain in the right upper quadrant. Ingestion of fatty foods precipitated and aggravated the attacks of pain in the right upper quadrant, which were accompanied by nausea and vomiting. Physical examination revealed marked tenderness in the right upper quadrant and epigastrium on abdominal palpation.

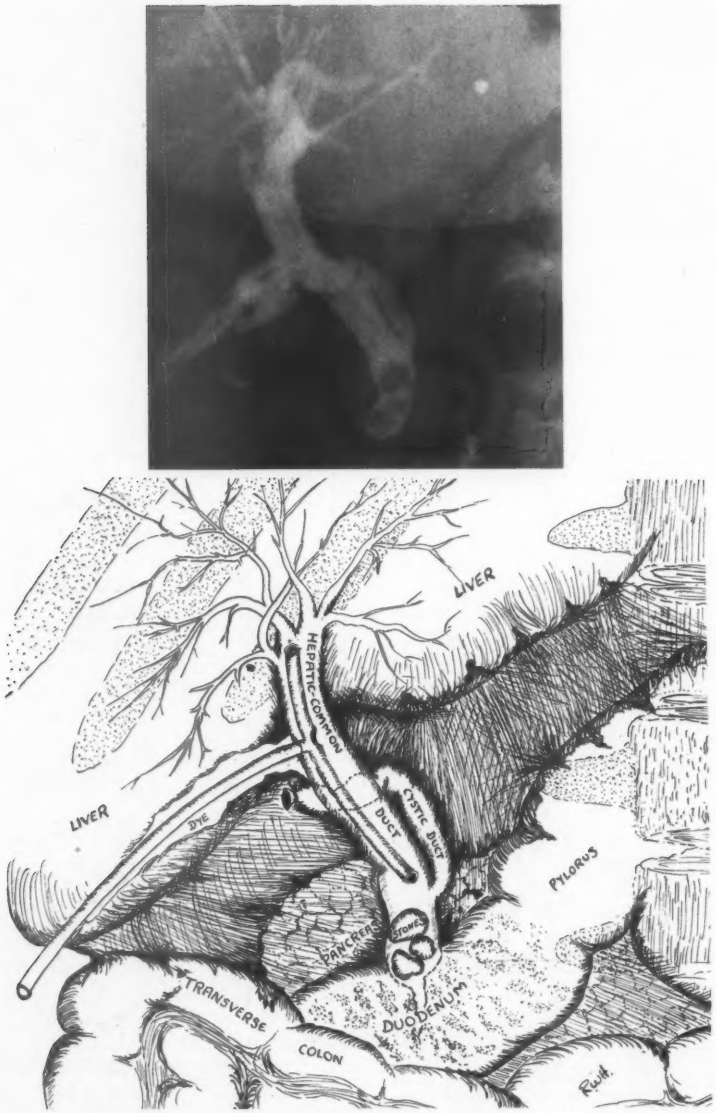

FIG. 2. T tube cholangiogram and sketch showing a long retrocholedochal cystic duct stump and three gallstones within the common duct.

Complete blood count, urinalysis and results of liver function tests were normal. An upper gastrointestinal series, barium enema, intravenous pyelograms and a chest roentgenogram revealed no abnormalities. Intravenous cholegraphin studies revealed a long cystic duct stump. Exploratory laparotomy on July 23, 1958, revealed multiple adhesions in the portal area with a cystic duct stump 2 inches long in parallel position to the common duct, surrounded by adhesions and several enlarged lymph nodes. Pathologic report showed chronic inflammation of the cystic duct stump. (Fig. 1.)

CASE II. A. M. (No. 632), a sixty-eight year old white woman, entered San Francisco Hospital on

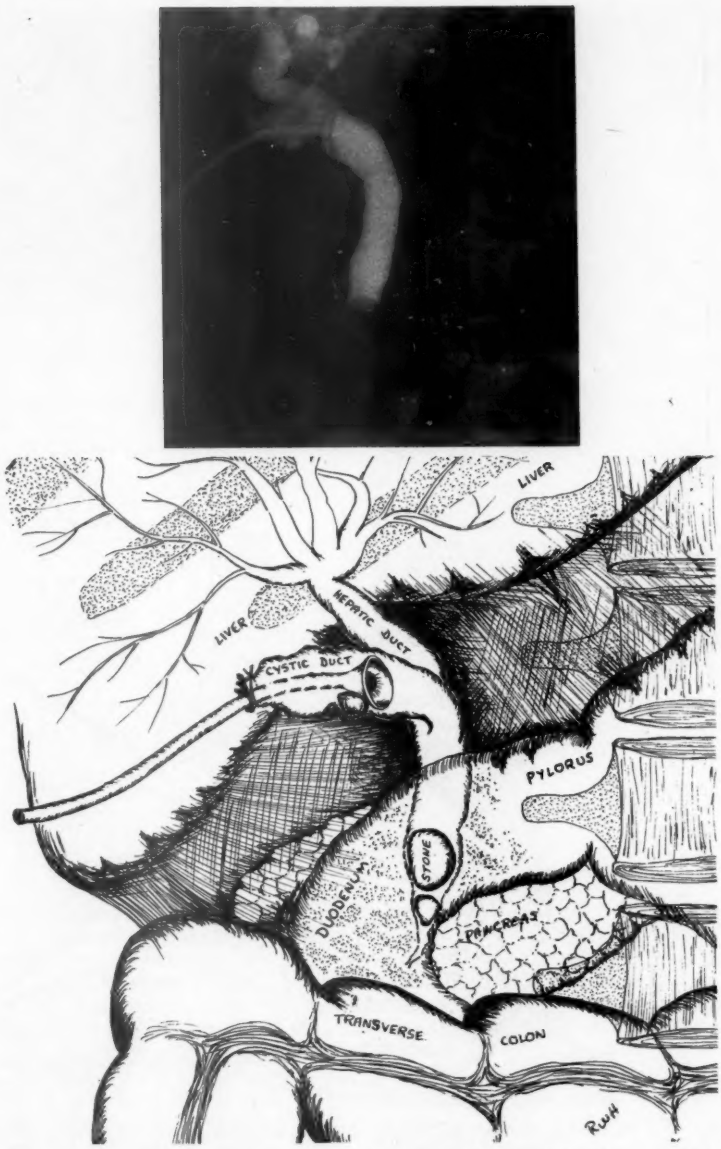

FIG. 3. Tube cholangiogram and sketch showing a gallstone within the cystic duct and gallstones within the common duct.

September 2, 1957, with a complaint of intermittent pain in the right upper quadrant, radiating to the right scapular area and associated with nausea and vomiting. Oral cholecystogram revealed gallstones and a poorly functioning gallbladder. Cholecystectomy and exploration of the common duct were performed September 24, 1957. Although the common duct was dilated, no stones were found except for the 14 gallstones in the gallbladder. A T tube was left within the common duct. Postoperatively the patient complained of almost constant nausea. Routine postoperative cholangiograms via the T tube ten days later revealed a very long and large cystic duct stump plus three

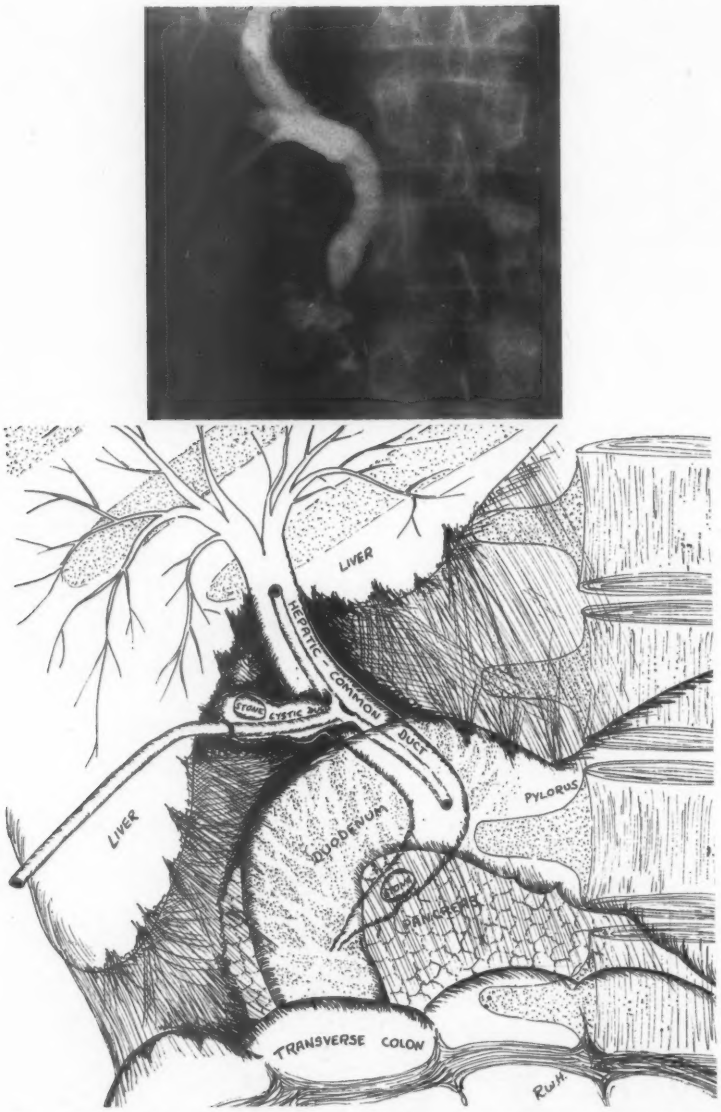

FIG. 4. T tube cholangiogram and sketch showing gallstone in cystic duct and gallstone within the common duct.

retained common bile duct stones. On October 5, 1957, re-exploration of the common bile duct obtained the three stones. The long cystic duct stump was found to enter the common bile duct within the substance of the pancreas, and therefore was not wholly excised. (Fig. 2.)

CASE III. H. O. (No. N19942), a sixty-four year old white woman, was admitted to San Francisco Hospital on July 24, 1955, with the complaint of pain in the right upper quadrant of several days' duration. Physical examination revealed severe pain and tenderness in the right upper quadrant in an elderly woman with jaundice. The bilirubin was 3.6 mg. per cent. A double dose Graham-Cole test and intravenous cholangiograms failed to show the gallbladder or the bile ducts. Cholecystectomy was performed on July 27, 1955, after exploration

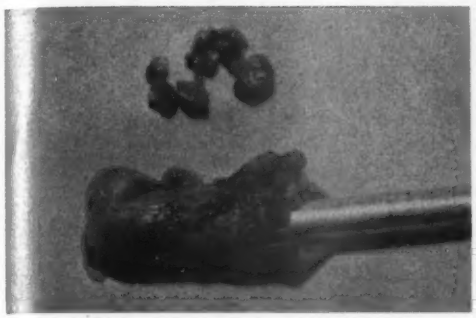

FIG. 5. Cystic duct stump and calculi which were contained within the stump.

revealed a perforated gallbaldder with gallstones. The common bile duct was explored through the stump of the cystic duct, and a mushroom catheter was inserted into the common duct via the stump. The pathological diagnosis was acute and chronic cholecystitis. Eleven days postoperatively, the patient had recurrence of severe pain in the right upper quadrant which radiated to the back and was associated with nausea and vomiting. Tube cholangiogram showed an impacted stone in the dilated cystic duct at its junction with the common duct. Repeat tube cholangiograms twenty-five days postoperatively revealed the stone to be in the common duct and the cystic and common ducts to be dilated. Ninety days after cholecystectomy, on October 8, 1955, a dilated cystic duct stump was excised, and a common duct stone was removed. The pathological report showed chronic imflammation of the cystic duct stump. (Fig. 3.)

CASE IV. A. D. (No. N136077), a seventy-six year old white man, entered San Francisco Hospital on July 10, 1956, with the complaint of nausea and vomiting of ten days' duration. Previously, on May 26, 1956, he underwent cholecystectomy following an acute exacerbation of chronic cholecystitis, which was manifested by a white blood cell count of 30,000 per cu. mm., and frank jaundice. At surgery the common duct was explored and operative cholangiograms were performed. Eight gallstones were removed from the common bile duct and several stones were within the gallbladder. The common duct was drained with a T tube. Postoperative cholangiograms via the T tube revealed a stone in the common duct and an impacted stone in the remnant of the cystic duct. Conservative treatment failed to dislodge the stone and the patient was discharged with laboratory evidence of liver damage and retained stones in the biliary tree. Upon entry ten days later, the patient had signs and symptoms of acute cholangitis. His hospital course was rapidly downhill, and he died on July 21, 1956. Autopsy revealed multiple liver abscesses, severe cholangitis and no stones in the bile ducts. (Fig. 4.)

FIG. 6. Photomicrograph of neuromas of sympathetic nerves on cystic duct stump of patient M. S. (Case v). Original magnification × 150.

CASE V. M. S. (No. E120493), a forty-eight year old white woman, entered Stanford University Hospital on October 30, 1954, referred by Dr. W. E. Fountain, for chronic attacks of pain in the right upper quadrant. The patient had a long history of indigestion and pain in the right upper quadrant, without jaundice. Stones were demonstrated and a cholecystectomy performed elsewhere in 1952. Since the operation the patient's symptoms have continued unabated, requiring narcotics for attacks of pain.

On physical examination, aside from the old scars (a cystocele and rectocele), no abnormalities were noted. The clinical impression was residual common duct stone. An attempt was made to visualize the stone by the use of cholegraphin. The common duct was demonstrated to be normal throughout and no stone noted.

On November 2, 1954, the right upper quadrant was re-explored. A stump of cystic duct, 3.5 cm., was found which contained small stones. The common duct was explored and appeared normal.

A T tube was left in the common duct and removed ten days later.

Microscopic examination of the tissue was abnormal only in that there were two large areas of proliferations of nerves as described by Womack and Crider [*11*].

Comment: In this case both alleged causes of pain were present. The stones were impacted in the stump of the cystic duct, and microscopically, a neuroma was present. It was of interest that although the common duct was demonstrated easily radiologically, the complete filling of the stump by stones prevented its demonstration. (Figs. *5* and 6.)

COMMENTS

There appears to be no doubt that a remnant of cystic duct may produce symptoms resembling cholecystitis and cholelithiasis. It is also evident that every patient in whom a long stump is left behind after cholecystectomy will not necessarily become symptomatic. The best explanation for the recurrence of symptoms would be the production of stones by the cystic duct remnant which then either by itself develops colic or passes the stones into the common duct. It is obvious that where no stones can be found, the possibility of a passed stone cannot be ruled out.

Two other possibilities should be considered. Stones in the common duct have been removed in patients in whom cholecystectomy was performed many years before and who have been asymptomatic in the interim. Bartlett and Quinby [*12*] in an excellent study of this problem had three patients whose common duct stones were removed seven, nine, and nineteen years after cholecystectomy. It is reasonable to assume that these were newly manufactured stones and not residual stones. These authors found that twenty-six of their ninety-two patients with recurrent symptoms after cholecystectomy were operated upon in their own hospital, so that they were quite confident of the technic used in the first operation. In only two patients, no stones were found and a cystic duct remnant was present.

The second possibility which should be considered when symptoms recur after cholecystectomy is the presence of a congenital variation in the extrahepatic biliary system overlooked at the first operation. The well known variation in the ductal system has been pointed out by many surgeons. The latest report by Hayes et al. [*13*] demonstrated some form of anomaly in 47 per cent of all cases studied. Evidence of this nature gives strong support for those who contend that operative cholangiography should be performed in every case.

Certainly no one could challenge the conclusion that the cystic duct should be ligated as closely as possible to its junction with the common duct.

SUMMARY

1. Five patients in whom recurrence of signs and symptoms of gallbladder disease developed following cholecystectomy are reported on.

2. The relationship of the symptoms to the cystic duct remnant is discussed.

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DISCUSSION

Carleton Mathewson, Jr. (San Francisco, Calif.): The majority of patients suffering from

cholelithiasis treated by cholecystectomy are symptom-free following operation. Dr. Cohn and Dr. Fibner have again focused our attention on that small percentage of patients who are not relieved of symptoms or who, after a period of relief, have symptoms simulating their original complaints.

Our observations to date have led us to believe that the persistence of symptoms or the recurrence of symptoms following cholecystectomy are usually due to one of three causes: (1) retained stones; (2) injury to the common duct; or (3) some condition other than cholelithiasis, having been responsible for the preoperative symptomatology, and not relieved at the time of surgery.

Apparently we must add to this list the occasional case of a retained remnant of the cystic duct. How frequently a remnant of the cystic duct is overlooked at the time of surgery, and in what percentage of cases the retained remnant will cause symptoms, will never be known.

The well known frequency of anomalies of the cystic duct in its relationship to the common duct, and the fact that these are often not apparent without meticulous and even hazardous dissection, makes it reasonably certain that a portion of the cystic duct not infrequently remains in place following cholecystectomy. It is reasonable to assume, however, that when a portion of the cystic duct is overlooked, the remnant in itself does not commonly cause persistent or recurrent symptomatology.

When symptoms do occur the cause is not always apparent. Pain is reported to be the most common symptom, and is often colicky in nature. Because of the type of pain, and the fact that jaundice is a common accompanying sign, it is reasonable to suspect that retained common duct stones or the development of stones in the remnant of the cystic duct is an important factor in the symptom complex. Certainly the five cases reported on today would tend to substantiate this point of view. No stones were demonstrated in only one of the five patients reported on.

If we can believe the interpretation of the postoperative cholangiograms in patient A. D. (case IV), who died as the result of severe cholangitis and multiple liver abscesses without demonstrable stones in the bile ducts at postmortem examination, then we must assume that the stones seen in the cholangiogram were passed in the interval before death. Certainly this is a likely explanation of the pre- and postmortem findings.

It is apparent from this report that a cystic duct remnant may be a contributing cause of symptoms simulating disease of the gallbladder and must be considered in the differential diagnosis of persistent or recurrent symptomatology following cholecystectomy. An ounce of prevention being better than a pound of cure, it is important that more emphasis be placed upon the common occurrence of the anatomical variations of the cystic duct in relation to the common duct, with the realization that it is indeed important to resect the cystic duct completely whenever it is possible to do so.

H. Glenn Bell (San Francisco, Calif.): I saw a patient who had undergone cholecystectomy at another hospital in December, 1956. In January, 1959 I reoperated upon him because he had typical symptoms of gallbladder disease. He had stones that were visible on a scout film of the abdomen. When we exposed this area, the usual adhesions were noted, but when we approached a healthy-appearing, normal-sized gallbladder and started to dissect down to the common duct, we found areas that were practically unexplored.

The previous surgeon had not been within 3 or 4 inches of the common duct. The patient must have had a very short and narrow connection between the fundus of the gallbladder and the lower part of the gallbladder. When the previous surgeon reached this short, what he called "cystic duct," he transfixed the duct at that point to avoid injury to the common duct. Before we completed surgery, we identified all the surrounding structures which is our normal procedure, that is, the cystic duct, common duct, cystic artery and right hepatic artery; it was apparent that they were all within normal limits.

Dr. Cohn suggested neuromas as perhaps being one of the causes of recurrent symptoms. Do we not find neuromas in every cystic duct when we remove the gallbladder and transfix or ligate the cystic duct? I believe that we would probably find neuromas in all such instances and that these neuromas do not produce the recurrent symptoms in the particular type of case under discussion.

The ones you really have trouble with as Dr. Cohn and Carl have mentioned, are those in which either stones in the ducts or residual infection is present.

One of my own patients upon whom I performed an original cholecystectomy had trouble seven or eight years later, not because of an enlarged cystic duct or re-formation of stones, but because of a granuloma that developed around the suture that we used to transfix the cystic duct.

Roy Cohn (closing): The question posed by Dr. Bell also occurred to us. We tried to review our autopsy series to determine the number of patients who had undergone cholecystectomy at some other time and died from other causes. Unfortunately the pathologist is not too interested in the surgeons' problems, and in none of these cases was a section of the cystic stump taken.

I am inclined to believe what Dr. Bell has stated is true.

Surgical Management of Chronic Pancreatitis

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IN the century that has passed since Le Dentu [1] performed the first surgical operation upon the pancreas, the multiplicity of surgical procedures that have been employed, and the reported dissatisfaction with many of these procedures, attests to the challenge offered to the surgeon by chronic pancreatitis. The inaccessible anatomical location of the pancreas, the technical hazards in dealing with the severely inflamed organ and the variable pathologic picture encountered at surgery have been among the important obstacles which have slowed progress in surgical management of this disease.

A better understanding of the pathologic mechanism and the anatomy of the pancreas, as well as refined diagnostic and surgical technics have served in recent years to encourage the surgeon in a bolder and more direct attack upon the diseased gland. The advent of cholangiography and pancreatography has not only aided in the surgical management of this disease, but also has served to give a clearer demonstration of the underlying disease, with particular reference to the presence or absence of obstruction of the duct of Wirsung. There is much evidence [2–4] to show that the symptoms as well as the underlying disease of the pancreas in chronic pancreatitis are directly related to obstruction of the pancreatic duct. There is further evidence to show that if ductal obstruction can be completely relieved, symptoms will be alleviated and pancreatic regeneration will occur, even in far advanced cases of pancreatitis [5].

At The Mason Clinic, fifty-eight operations have been performed since 1946 on thirty-nine patients with chronic relapsing pancreatitis. In the group of patients with disease of the biliary tract and secondary pancreatitis, there were eighteen patients in whom thirty operations were performed. At least nine different technics (Table 1) have been used usually in combination. Many of these patients had had previous indirect surgical procedures which had been inadequate for the relief of pancreatitis. The most commonly used indirect procedure for pancreatitis in our series has been cholecystectomy, with exploration of the common duct and removal of common duct stones, combined with dilatation of the sphincter of Oddi. In the earlier, milder forms of secondary pancreatitis, these procedures will often relieve the patient. In our experience these methods have failed in the presence of pancreatic ductal obstruction. At the time of exploration of the common duct, the surgeon can determine the presence or absence of pancreatic ductal obstruction by a reflux pancreatogram (Fig. 1), which may show not only the duct of Wirsung but also the duct of Santorini emptying separately into the duodenum. Such a pancreatogram gives definite evidence of a clear pancreatic ductal system. If the surgeon cannot clear the pancreatic duct, and fibrosis of the sphincter of Oddi is encountered during the exploration of the common duct, a sphincterotomy should be performed. At the time of sphincterotomy, the

TABLE 1
INDIRECT BILIARY TRACT PROCEDURES FOR SECONDARY PANCREATITIS

1. Cholecystectomy
2. Exploration of common duct and dilatation of sphincter
3. Exploration of duct of Wirsung
4. Exploration of duct of Santorini
5. Division of sphincter of Oddi
6. Choledochojejunostomy, Roux-Y
7. Gastrojejunostomy (obstructed duodenum)
8. Vagotomy
9. Excision of cystic duct stump

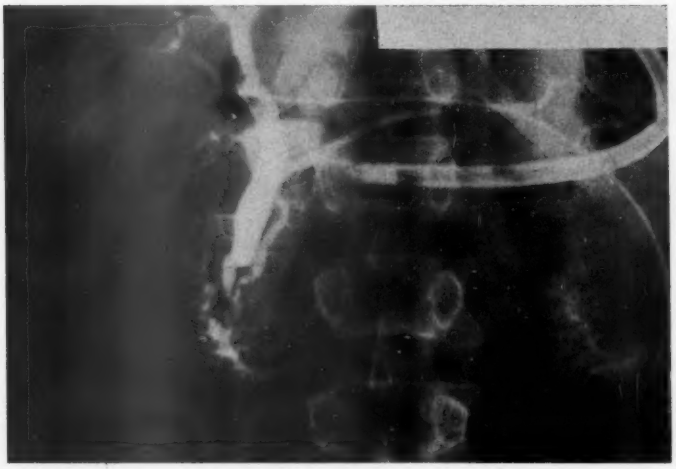

FIG. 1. Reflux pancreatogram.

duct of Wirsung can be evaluated either by passage of a polyethylene tube the full length of the duct or by cannulation of the duct and performing a direct pancreatogram. (Fig. 2.) If stones or strictures are encountered during these diagnostic procedures, further surgery is mandatory to relieve the pancreatitis. In nine of eighteen patients treated by indirect methods, the pancreatic duct was demonstrated either by pancreatogram or found to be clear by actual probing of the pancreatic duct and passage of a polyethylene tube the full length of the duct of Wirsung. In one additional patient, the duct of Santorini was demonstrated. A sphincterotomy on the opening of the duct was performed and the duct explored and found to be clear.

An analysis (Table II) of the results in this group shows that the result was considered good in ten patients, fair in five, and poor in three. The most consistent good results were obtained in patients in whom the pancreatic duct could be demonstrated to be clear of obstruction and in whom the sphincter of Oddi was either dilated with the largest Bakes dilator or divided by transduodenal sphincterotomy. Poor results were obtained in patients with calcinosis of the pancreas and in patients in whom the pancreatic duct was not cleared at the time of surgery.

TABLE II
RESULTS OF INDIRECT BILIARY TRACT PROCEDURES FOR SECONDARY PANCREATITIS
(EIGHTEEN PATIENTS—THIRTY OPERATIONS)

Good	10
Fair	5
Poor	3*

* Two patients alcoholic; one with hemachromatosis.

Patients who continue excessive use of alcohol present a group in whom the result is invariably poor, regardless of the type of surgery used. Two patients, classified as having a poor result, continued excessive intake of alcohol and diabetes developed as well as recurring attacks of pancreatitis.

From this experience with indirect procedures, we are impressed with the importance of demonstrating the pancreatic ductal system, and of clearing not only the biliary system of all obstruction and stones but also the pancreas, either by direct probing or by pancreatogram. A review of the literature would indicate that few surgeons have stressed the importance of adequately relieving obstruction of the pancreatic ductal system. It is only reasonable to conclude that biliary tract procedures, including sphincterotomy, have little or no relationship to actual pancreatic ductal obstruction. It follows that indirect procedures cannot be applied successfully when chronic pancreatitis is so far advanced that pancreatic obstruction is present, and recurring attacks

FIG. 2. Direct pancreatogram.

are no longer dependent upon disease of the biliary tract. It would appear, therefore, that sphincterotomy and other indirect procedures are successful only when employed in early secondary pancreatitis with demonstrable disease of the biliary tract, before obstruction of the duct of Wirsung develops.

We are well aware of the hazards of pancreatography. Injection of dye into the duct of Wirsung must be done without pressure and with as little trauma as possible. The surgeon should familiarize himself with the technics on cadavers prior to attempting them clinically.

In contrast to those patients with disease of the biliary tract and secondary pancreatitis, there is the group of patients with primary pancreatitis in whom disease of the biliary tract is either absent or inconspicuous. Primary chronic pancreatitis may result in obstruction and cyst formation or in pancreatic fibrosis and calcinosis with abscess formation. In the group of patients with pancreatic cysts, twenty operative procedures were performed on sixteen patients. There were nine pseudocysts and seven inflammatory cysts of the pancreas proper. (Table III.) In the large pseudocysts, marsupialization is often the only feasible procedure. Marsupialization alone may be curative in those patients in whom the duct communicates with the unobstructed duct of Wirsung. (Fig. 3.) One of the largest cysts encountered in this series, measuring 20 cm. in diameter, was treated by simple marsupialization with a Pezzer catheter. A pancreatocystogram performed one month after operation demonstrated that the cyst communicated with an unobstructed duct of Wirsung. The catheter was left in place eight months, during which time the large epigastric mass disappeared and the symptoms of pancreatitis subsided. The Pezzer catheter was removed eight months after the initial operation, the sinus tract closed within the week, and the patient has remained free of symptoms of pancreatitis for five years following surgery. In three additional patients, marsupialization was curative and the patients have been relieved of all

TABLE III
DIRECT PROCEDURES FOR PRIMARY PANCREATITIS
(PANCREATIC CYSTS)

Pseudocysts	
Marsupialization	9
Cysts of pancreas	
Cystoduodenostomy	3
Cystojejunostomy, Roux-Y	2
Pancreatoduodenectomy	1
Excision of cyst of tail (distal pancreatectomy)	1

symptoms of pancreatitis. In the remaining five patients with pseudocysts, results in two were fair, in one poor, and two patients died. Those patients who continue to have symptoms of pancreatitis and in whom the marsupialization tract fails to close, or closes only intermittently and reopens following exacerbation of pancreatitis, should have a more definitive surgical procedure to erradicate the fistula.

The two patients who died, did so at four years and nine years following operation of causes unrelated to pancreatitis. One died following an accident, the other of a stroke. During the interval following operation, both patients had intermittent attacks of mild abdominal pain.

Marsupialization should be reserved for those patients in whom cysts are too large to be dealt with by any other means. Prior to removal of the Pezzer catheter, utilized in marsupialization, an injection of dye into the cyst should be performed to determine the presence or absence of communication of the cyst with the pancreatic duct. In the event that this communication can be demonstrated, removal of the Pezzer catheter and observation for subsidence of the symptoms of pancreatitis for a period of several months is indicated prior to any further surgery.

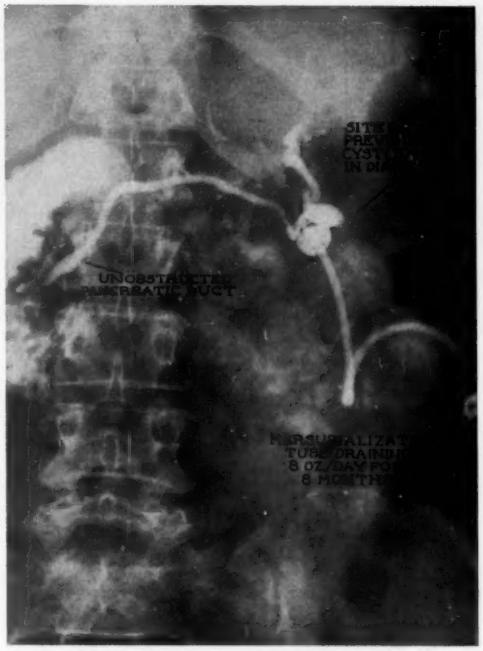

FIG. 3. Large pseudocyst which subsided with marsupialization.

In the second group there were seven inflammatory cysts of the pancreas proper. Four of these were located in the head of the pancreas, two in the body and one in the tail of the pancreas. Three of the four patients with cysts located in the head of the pancreas were treated by internal drainage into the duodenum. (Fig. 4.) All three of these cysts were drained into the duodenum through a large opening, suturing the lining of the cyst to the mucosa of

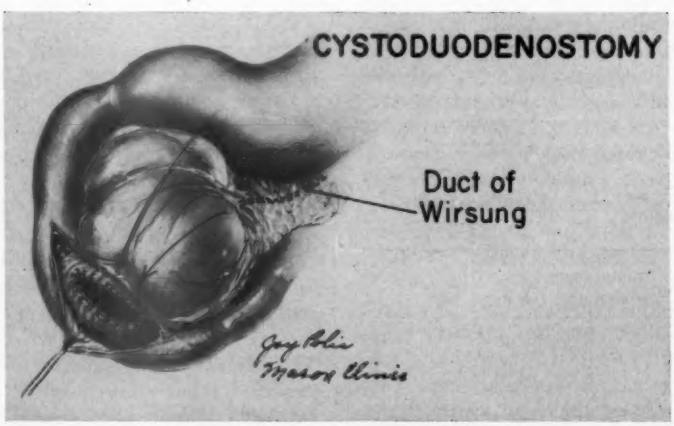

FIG. 4. Cyst of head of pancreas.

TABLE IV
RESULTS OF DIRECT PROCEDURES FOR PRIMARY PANCREATITIS
(PANCREATIC CYSTS, SIXTEEN PATIENTS—TWENTY OPERATIONS)

Good	9
Fair	2
Poor	1
Dead	4*

* Early postoperative deaths, one; late postoperative deaths, three (nine years, four years and four and a half years postoperatively), of alcoholism and cirrhosis.

the duodenum. The stoma varied from 1 cm. in diameter in the smallest to 5 cm. in the largest. These patients have been followed up for eight, three and two years, respectively, and remain free of symptoms. The result in all three patients was classified as good, in spite of the fact that one patient had extensive calcification in addition to a cyst of the head of the pancreas.

In one patient with multilocular cyst of the head of the pancreas, a pancreatoduodenal resection was performed. In this patient intestinal obstruction developed approximately six weeks after surgery, requiring a second operation. This patient died of empyema and multiple liver abscesses eight weeks after the initial surgery. This represents the only operative death in the entire series.

Two patients with cysts located in the body of the pancreas were treated by cystojejunostomy. In the second patient a Roux-Y cystojejunostomy was performed for a large cyst located in the mid-portion of the pancreas and extending into the gastrohepatic ligament and transverse mesocolon. It is pertinent that a year prior to the cystojejunostomy the patient had had a cholecystectomy, choledochotomy and sphincterotomy which failed to relieve the symptoms of pancreatitis. Following the definitive cystojejunostomy, the patient gained weight and, seven years after the operation is still free of symptoms. In the second patient, a 15 by 12 cm. cyst with 500 cu. cm. of fluid was found at the time of surgery. In addition, the patient had advanced biliary cirrhosis. A Roux-Y pancreatocystojejunostomy was performed. The patient continued an excessive alcohol intake with resulting recurrent attacks of pancreatitis and progression of the biliary cirrhosis. He died four years after the operation.

In one patient with a cyst of the tail of the pancreas, complete excision of the cyst with distal pancreatectomy was performed. This patient has been followed up for three years and is entirely free of attacks of pancreatitis.

In this group of patients with pancreatic cysts, twenty operations of five general types were utilized in sixteen patients. (Table IV.) It is obvious that the best results are obtained in patients in whom a definitive procedure, which either removes the cyst or entirely relieves the obstruction of the pancreatic ductal system, is performed. In performing internal drainage on a cyst, the surgeon must be aware that the cyst may be secondary to obstruction by a carcinoma [6]. One should rule out the presence of malignancy before relying on simple drainage of a cyst.

Pancreatic fibrosis and calcinosis represents a third group of patients with chronic pancreatitis which are perhaps the most difficult to manage surgically. In our experience, pancreatic calculi occur within the ductal system, much as biliary tract stones occur within the biliary radicles. This has been demonstrated by the excellent dissection of Edmondson [2]. This is in contrast to the opinion that calculi occur within the pancreatic parenchyma rather than the ductal system, as suggested by Puestow [7]. The presence of these stones necessitates a direct surgical attack on the pancreas with complete clearance of the duct for relief from chronic pancreatitis. In this group there were five patients in whom eight surgical procedures were carried out. (Table V.) The seriousness of pancreatic calcinosis and fibrosis is clearly indicated by the fact that a number of pioneers in pancreatic surgery, including Longmire [8], Cattell and Warren [4],

TABLE V
PROCEDURES FOR FIBROSIS AND CALCIFICATION

Distal pancreatectomy with Roux-Y pancreaticojejunostomy	1
Pancreatoduodenectomy	3
Pancreaticojejunostomy	1

RESULTS
(FIVE PATIENTS—EIGHT OPERATIONS)

Good	3
Fair	1
Dead	1*

* Late, due to alcoholism.

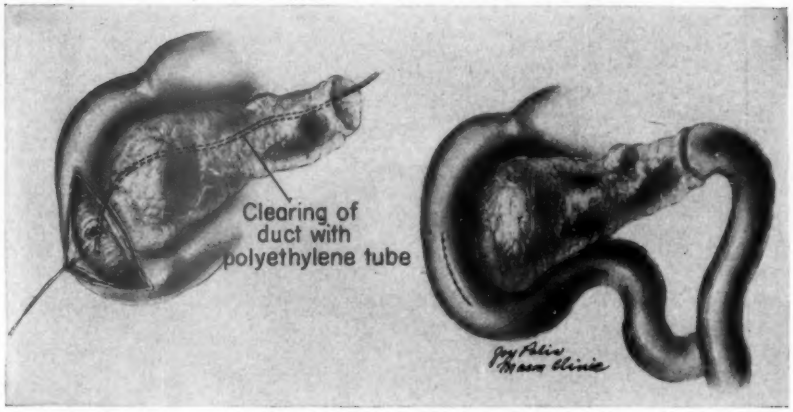

FIG. 5. Distal pancreatectomy with pancreaticojejunostomy.

Claggett [9] and others have advocated total pancreatectomy for far advanced cases. In one patient in this group, fibrosis and calcinosis was limited largely to the tail of the pancreas. A distal pancreatectomy and a Roux-Y pancreaticojejunostomy was performed. (Fig. 5.) The patient also had a stricture of the common bile duct requiring sphincterotomy. The duct of Wirsung was cleared by passage of a polyethylene tube the full length of the duct. This patient is well, one and a half years following surgery.

Three patients in this group had pancreatic fibrosis and calcinosis largely involving the head of the pancreas. In these patients it may be difficult to rule out the presence of carcinoma. Longmire [8] found this to be a problem in two of his cases, even after frozen section was obtained at the time of operation. In two of three patients in our series, carcinoma could not be ruled out. In addition, the pancreatic duct as well as the common bile duct was obstructed. Therefore, pancreatoduodenectomy was obviously the only procedure feasible. All three patients survived the operative procedure, and two are alive ten years and three years following surgery. One of these patients required reexploration of the common bile duct eighteen months after the resection. Three years later, cholecystectomy and choledochotomy with T tube drainage was performed. For the last five years this patient has been relatively free of attacks of chronic pancreatitis. The third patient in this group had a large mass of the head of the pancreas, which encroached upon the superior mesenteric artery. Complete resection necessitated removal of a large segment of small intestine along with the superior mesenteric artery. This patient survived five years after surgery but remained an alcoholic; he died of alcoholism and malnutrition.

A more complex problem is presented by patients who have multiple points of obstruction from both stricture and stones. In one such patient with calcinosis and multiple strictures the pancreatic duct was incised over a 10 cm. area along its long axis. (Fig. 6.) Multiple large stones were removed and the duct was cleared in its entirety by the use of scoops. The strictures were dilated by large Bakes dilators all the way to the tail of the pancreas and proximally into the duodenum through the duct of Santorini, which was the only communication between the pancreatic ductal system and the duodenum. Following this a Roux-Y pancreaticojejunostomy with a large stoma was performed. This patient, prior to surgery, was a partial narcotic addict; he had lost some 80 pounds and was having almost continuous severe epigastric and back pains. Diabetes had also developed and he required insulin therapy. A year and a half after surgery, this patient was still entirely free of symptoms. He had gained weight and had been treated with small doses of Orinase® instead of insulin. His stools no longer have the characteristics of steatorrhea, indicating at least some improvement in pancreatic function.

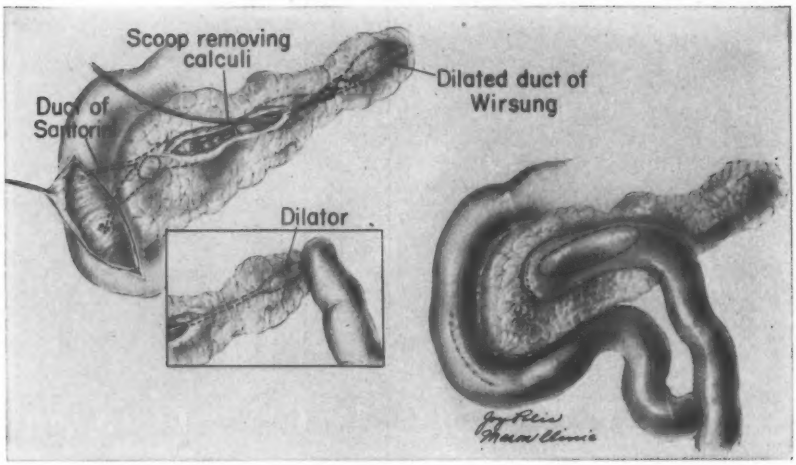

FIG. 6. Pancreaticojejunostomy.

COMMENTS

The choice of surgical therapy in far advanced chronic pancreatitis with ductal obstruction lies between removal of diseased tissue by resection, and complete clearance and adequate drainage of the pancreatic ductal system with preservation of pancreatic tissue. The argument as to which of these methods is superior will only be settled when we can answer two questions. One, will pancreatic tissue relieved of obstruction show regeneration? And two, will an adequately cleared and adequately drained pancreatic duct remain open over long periods of time? Present evidence, as pointed out by Mullholland and Doubillet [5], Puestow [7] and others indicate that pancreatic tissue will regenerate when relieved of obstruction. Mullholland stresses that this can be shown by both biopsy and serial secretin tests. In our experience an adequately drained pancreatic duct has remained open as long as nine years with complete relief of pancreatitis. These facts strengthen our preference at the present time for adequate drainage of the pancreatic ductal system with preservation of pancreatic tissue whenever feasible. We reserve resection for difficult cases, particularly with fibrosis of the head of the pancreas with obstruction of the common duct and the duct of Wirsung, and when carcinoma cannot be ruled out.

SUMMARY

1. Fifty-eight operative procedures in thirty-nine patients with chronic pancreatitis are reviewed.

2. The most consistent good results were obtained in patients in whom a clear pancreatic ductal system was demonstrated at the time of surgery.

3. Adequate internal drainage procedures, coupled with pancreatic ductal clearance, have yielded good results up to nine years after surgery.

4. Indirect procedures, such as sphincterotomy, are successful only in early cases of pancreatitis with disease of the biliary tract. Sphincterotomy will fail in most cases in the presence of pancreatic ductal obstruction if the obstruction is not relieved.

5. In the thirty-nine cases reviewed, there was one operative death and eight late deaths. In four of the eight late deaths, the patient continued the use of large amounts of alcohol.

6. Our preference at the present time is clearance of the pancreatic ductal system with adequate internal drainage, and preservation of functioning pancreatic tissue whenever feasible.

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DISCUSSION

WILLIAM P. LONGMIRE, JR. (Los Angeles, Calif.): I am pleased to discuss this most interesting and informative paper of Drs. Hill, Stone and Baker. This account of their experiences in the treatment of thirty-nine patients with chronic pancreatitis contains much valuable information which I am certain will be of help to all of us in the management of the difficult problems related to this disease.

For purposes of discussion, the authors have classified their cases essentially into three groups: (1) cases associated with diseases of the biliary tract; (2) pancreatic cysts; and (3) fibrosis and calcification of the pancreas.

They have emphasized obstruction of the pancreatic duct as the most important single factor related to the symptoms and pathology of chronic pancreatitis.

From the standpoint of prognosis and treatment, our experiences with this disease have led us to place a somewhat different emphasis on various aspects of the over-all problem.

The initiating or etiological factor, it would seem, is of utmost importance. In our experience, the majority of patients who have pancreatitis solely on the basis of associated disease of the biliary tract will be relieved of their symptoms by cholecystectomy and choledocholithotomy. It is conceivable that in some patients who have had stones lodged at the ampulla of Vater or who have passed multiple small stones, stenosis of the sphincter of Oddi may develop and, thereby, they would benefit from sphincterotomy. It is difficult to ascribe any particular therapeutic value to pancreatograms, probing or passing a polyethylene tube the length of the duct of Wirsung. The most common type of chronic pancreatitis in our experience has been that associated with chronic alcoholism. All varieties of pathological states may be associated with "alcoholic pancreatitis"—fibrosis, lithiasis, calcinosis and cyst formation.

Observations on the course of these patients have led us to believe that this is an essentially diffuse disease of the parenchyma and finer distal duct radicles of the gland. Obstructions within the duct of Wirsung, whether they be single or multiple, are rarely the primary cause of recurrent attacks of pancreatitis associated with alcoholism. That such obstructions do occur cannot be doubted and the "chain of Lakes" appearance of the ductal system demonstrated in the pancreatograms described by Puestow and Gillesby is a common finding. There seems little reason to believe, however, that such scarring and stenosis will be confined to the duct of Wirsung. It would seem much more probable that such widespread alterations in this ductal system would also extend into the secondary and distal ductal system as well.

If this view of the nature of the pathology of pancreatitis associated with alcoholism is correct, relief of symptoms could rarely be expected from any procedure which is designed merely to provide more adequate drainage of the major duct of Wirsung. Indeed, in the two cases in which we have utilized a caudal pancreatic jejunal anastomosis, the course of the disease was unaltered.

In trying to apply a rational treatment for chronic pancreatitis, the source of the pain is also another important but confusing aspect which must be considered. Again, it must be concluded that distention of the pancreatic ductal system *may* cause pain but it does not always do so. For example, in operations for painless jaundice during which carcinoma of the head of the pancreas is found, there is usually increased fibrosis of the pancreas, microscopic evidence of chronic pancreatitis, and dilatation of the ductal system—in some cases to a fairly marked degree—yet such patients may have been totally free of pain.

It has been our belief that, once the disease has progressed to the chronic stage with gross architectural changes in the gland, the involved portion actually acts as a sequestrum, a nidus of active inflammation, and that this inflammatory process in itself may be the site of origin of pain either with or without associated ductal obstruction. If this interpretation is correct when the disease process has progressed to this stage, excision of the inflammatory area is the only procedure which may be expected to give symptomatic relief regularly. In evaluating the indications for, and the anticipated results from, any type of therapy for chronic pancreatitis associated with alcoholism, the psychopathological accompaniments of this disease must be recognized. In a study of twenty white male pa-

tients at the Veterans Administration Hospital, Providence, Rhode Island, Lawton and Phillips [6] noted that thirteen of twenty patients had, at one time or another, been hospitalized in the neuropsychiatric service of Veterans Administration hospitals; of these, ten were diagnosed as suffering from a psychiatric disability prior to receiving the diagnosis of chronic pancreatitis.

It must also be remembered that diffuse calcification of the pancreas and other pathological changes associated with chronic pancreatitis may occur in totally asymptomatic individuals.

Such considerations have made us conservative in our selection of patients for operation when pancreatitis is associated with alcoholism.

JOEL W. BAKER (Seattle, Wash.): It is a disturbing responsibility to operate for chronic pancreatitis, the etiology of which is unknown, possibly varied, and the treatment therefore controversial. In our small series, reviewed by Dr. Hill, the results leave much to be desired. The best results are obtained in patients with recurring acute attacks spaced by longer intervals of comfort. In these patients with associated disease of the biliary tract, usually common duct stone or fibrosis of the sphincter distal to a common passage, the results in general are good if the process has not created chronic changes in the pancreas. Even without demonstrable disease of the biliary tract, Doubilet has reported good results with sphincterotomy in 90 per cent of his cases provided the pancreatic duct is not obstructed. Unfortunately, in the advanced chronic phase of the disease, the pancreatic duct is more often involved, granted that the initiating force may have been biliary reflux. The pancreas is often either small or fibrocystic; sometimes a dilated pancreatic duct can be seen along its ventral surface. The point we wished to emphasize has been made previously by Howard Gray, Longmire, Duval and Jonathan Rhoades, and others, that is, that certainly in these cases, partial obstruction of the pancreatic duct must be relieved. Even in the earlier stages, involvement of the pancreatic duct cannot be ruled out; the pancreatic duct must be cannulated and pancreaticograms made when sphincterotomy is performed for relapsing pancreatitis, if we are not to overlook primary obstructions in the pancreatic duct itself. If the opening of the pancreatic duct cannot be visualized in the ampulla at the time of sphincterotomy, it means either there is not a common passage or it has been strictured; hence, further search for the opening of the pancreatic duct into the duodenum must be made. In answer to Dr. Longmire, there is of course no therapeutic value in the pancreaticogram *per se*, only in that it may lead to the discovery of the true underlying pathogenesis in some cases.

In patients with the debilitating chronic phase of the disease with constant pain and weight loss, sometimes with steatorrhea and diabetes, often even with addiction to alcohol or narcotics, or both, indirect attacks such as sphincterotomy are not enough. In such patients a direct attack on the pancreas must be made. In patients with a dilated pancreatic duct we would prefer to try to clean out the pancreatic duct and anastomose it rather than to sacrifice further pancreatic tissue by removal. The Roux-Y anastomosis of the jejunum to the duct is technically less hazardous as well as less sacrificing. This however applies only to those patients with a dilated duct—not to those with diffuse calcinosis. Occasionally, because of multiple small abscesses that cannot be adequately drained, diffuse calcinosis, or because cancer cannot be ruled out, an amputation of either the head or the tail of the pancreas may be unavoidable.

In assaying the results of the various recommended modalities for treatment, we should clearly differentiate those with several attacks of acute edematous pancreatitis associated with disease of the biliary tract from those with recurring attacks unassociated with disease of the biliary tract and from those with the chronic phase of the disease with constant distress and weight loss. In this latter group, we are dealing with a pancreas that has been partially destroyed and probably irreversibly so. As in dealing with strictures of the common bile duct, the patient may have to accept repeat operations to clean out the pancreatic duct, dilate its strictures and insure decompression of the obstruction. The wider anastomosis along the length of the duct may be less prone to recurrent obstruction than the cross section of the duct. When these measures fail, resection of the pancreas is the only procedure left. The alcoholic will not be restored by any of these procedures.

CARLETON MATHEWSON (San Francisco, Calif.): You have already heard a good many comments about the difference in disease in patients admitted to the General Hospital in San Francisco and in patients admitted elsewhere. This apparently applies also to pancreatitis.

We have been interested in this problem for some years and, I must say, have been greatly distressed with our results. At times we are encouraged by the enthusiasm about methods of treatment that have been advocated elsewhere. Yet these seem almost universally to fail in our hands. It seems also that we are the melting pot for patients who have wandered away from their original treatment, and have ended up in our hands.

Over the years we have been impressed with the fact that, in our hospital at least, the majority of these patients are alcoholics. If you can cure the

alcoholism, which we seem unable to do in the greatest number of instances, you can very often cure the pancreatitis. That is, if you see the patients who have early pancreatitis as a result of chronic alcoholism, and if you can get them to stop drinking, the metabolic disease which causes the pancreatitis seems to be abated and the patients get better.

We always look for a simple answer to a difficult problem and the simplest solution to this problem would seem to be to establish drainage when a stricture is present. I would like to point out the fact that it was the primary metabolic disease that caused the strictures, and if the disease continues the formation of strictures will continue. Simple drainage does not relieve the primary disease. I would like to emphasize what Dr. Longmire has pointed out, and that is that these strictures are generally not single strictures but multiple. The disease involves the entire ductal system out into the periphery of the gland, even though you may relieve a portion by dilatation, retrograde or other types of drainage of the main ductal system, this does not influence the strictures that are out in the parenchyma of the gland. When you open these glands at autopsy and see the extent of the disease and the calcinosis throughout the peripheral ductal system, it makes you dubious about the effectiveness of any simple method of drainage.

We have found in chronic cases that patients with persistent pain often do become addicts and the only method of relief is subtotal or total pancreatectomy. This would seem to be a radical approach to the problem, but this is a problem that must be approached radically.

I would like to make mention of the pseudocysts of the pancreas. Dr. Pinkham reviewed the pseudocysts at our hospital many years ago, and in the majority of these cases they were relieved by marsupialization. However, we have found that these cysts will often drain for as long as two years. When the cyst is thick-walled, inaccessible, and not resectable, internal drainage is an excellent method of treatment provided the cyst is drained with a defunctionalized loop of bowel.

Roland D. Pinkham (Seattle, Wash.): I would like to relate a case history that supports quite graphically the views of Doctors Longmire and Mathewson. I operated upon this patient several years ago. However, he has had recurrent episodes of pancreatitis, I believe seven in all, over a period of ten or eleven months. At the time of surgery, we were unable to tell whether this man had a large neoplastic mass in the head of the pancreas or a huge inflammatory mass.

A modified Whipple procedure was performed, the head and body of the pancreas and duodenum were resected and the tail of the pancreas was reimplanted into the transected end of the jejunum. The microscopic and macroscopic examination of the resected lesion showed it to be a severely inflamed segment of pancreas with a markedly dilated and thickened duct with a stricture just distal to the junction of the duct of Wirsung and the common duct. The patient did quite well for one and one-half to two years. After the first operation I learned that this man had been an alcoholic. He again had attacks of abdominal pain with marked elevation in serum amylase, and after the third such attack, it was decided to reoperate. At the time of the second operation the tail of the pancreas was edematous and inflamed. It was removed and the proximal jejunum was closed. We had presumed a stricture of the duct of Wirsung had developed at the site of implantation into the jejunum. Much to our amazement, examination of the specimen showed no stricture and no dilatation of the duct, only an area of focal pancreatitis in the remaining tail segment. It developed that the patient's recent attacks followed overindulgence in alcohol.

I believe, as Doctor Mathewson stated, that the stricture usually follows the bouts of pancreatitis which in almost every case of recurring pancreatitis is due to alcohol. The occurrence of the stricture no doubt aggravates the disease, but the real cure can be found only in the control of alcohol ingestion.

Lucius D. Hill (closing): When we asked Dr. Longmire to discuss this presentation we knew he was in favor of resection of the pancreas, and believed that it would give all of us an opportunity to hear the other side of the problem presented by a pioneer in pancreatic surgery.

I certainly do agree, and I know Dr. Baker and Dr. Stone agree with me, that patients who continue to indulge in large quantities of alcohol will have a poor result no matter what type of surgery is performed.

We have been fortunate in having a number of patients who were either not addicted to alcohol prior to surgery or have refrained from the use of alcohol since surgery.

Dr. Longmire has very ably presented some beautiful evidence favoring resection of the pancreas. We do believe, however, that in hands less capable than Dr. Longmire's, total pancreatectomy may not always be wise. Pancreato-duodenal resection by and large will carry a somewhat increased mortality and morbidity rate over and above the mortality and morbidity rate associated with internal drainage procedures. We are watching the patients who have had internal drainage procedures quite eagerly in the hope that their symptoms will be relieved over long periods of time.

As we had hoped to bring out in this paper the

last chapter in this type of surgery has not been written and certainly Dr. Longmire's evidence is quite strong for pancreatic resection.

We appreciate the comments of Dr. Mathewson and again agree that patients who are alcoholics are not going to derive any benefit from surgery for chronic pancreatitis.

We do not wish to imply that pancreatography or cannulation of the pancreatic duct has any therapeutic benefit whatever—these are simply diagnostic tools. I appreciate Dr. Pinkham's discussion of his interesting case.